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THE LANCET

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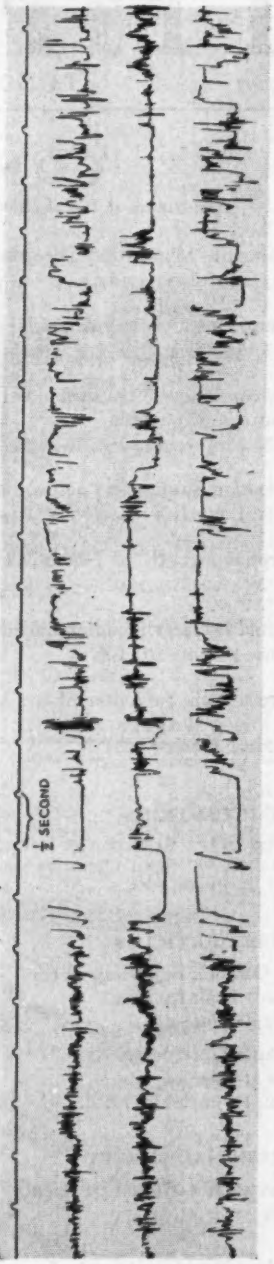

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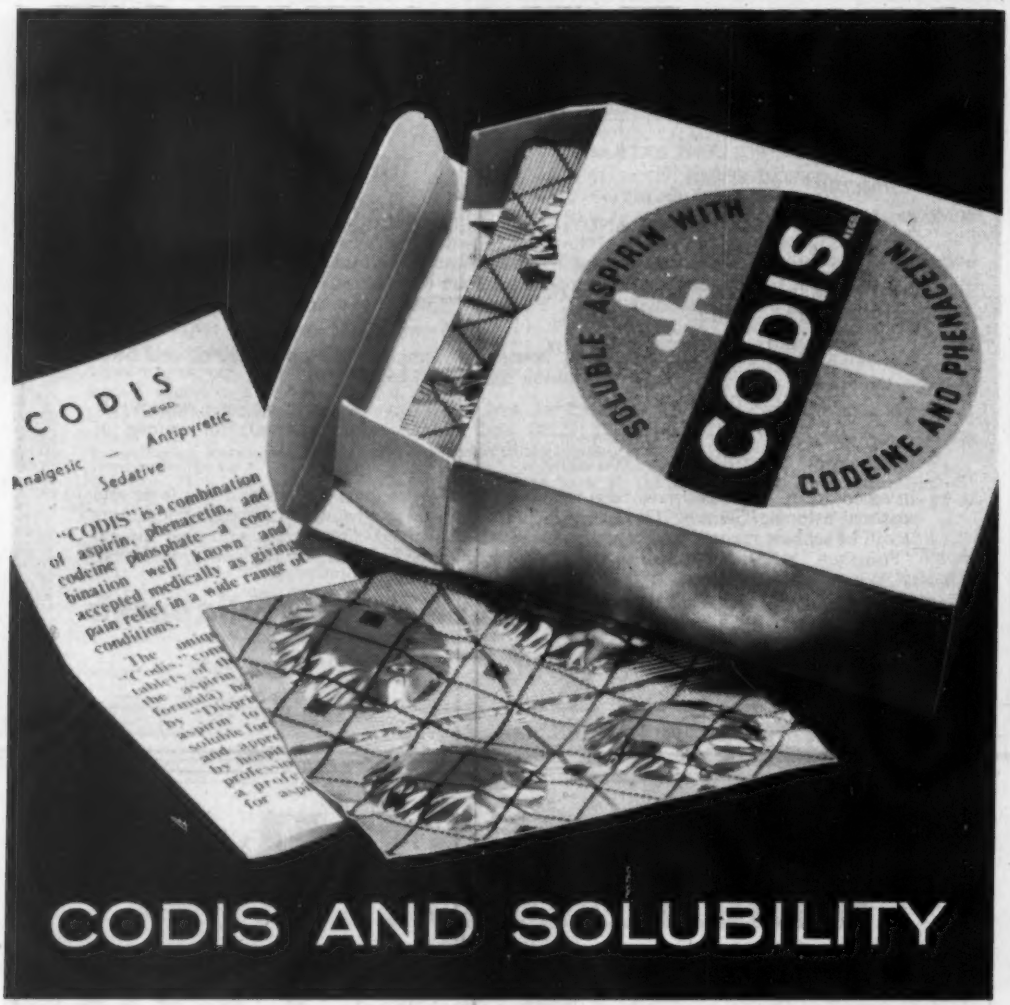
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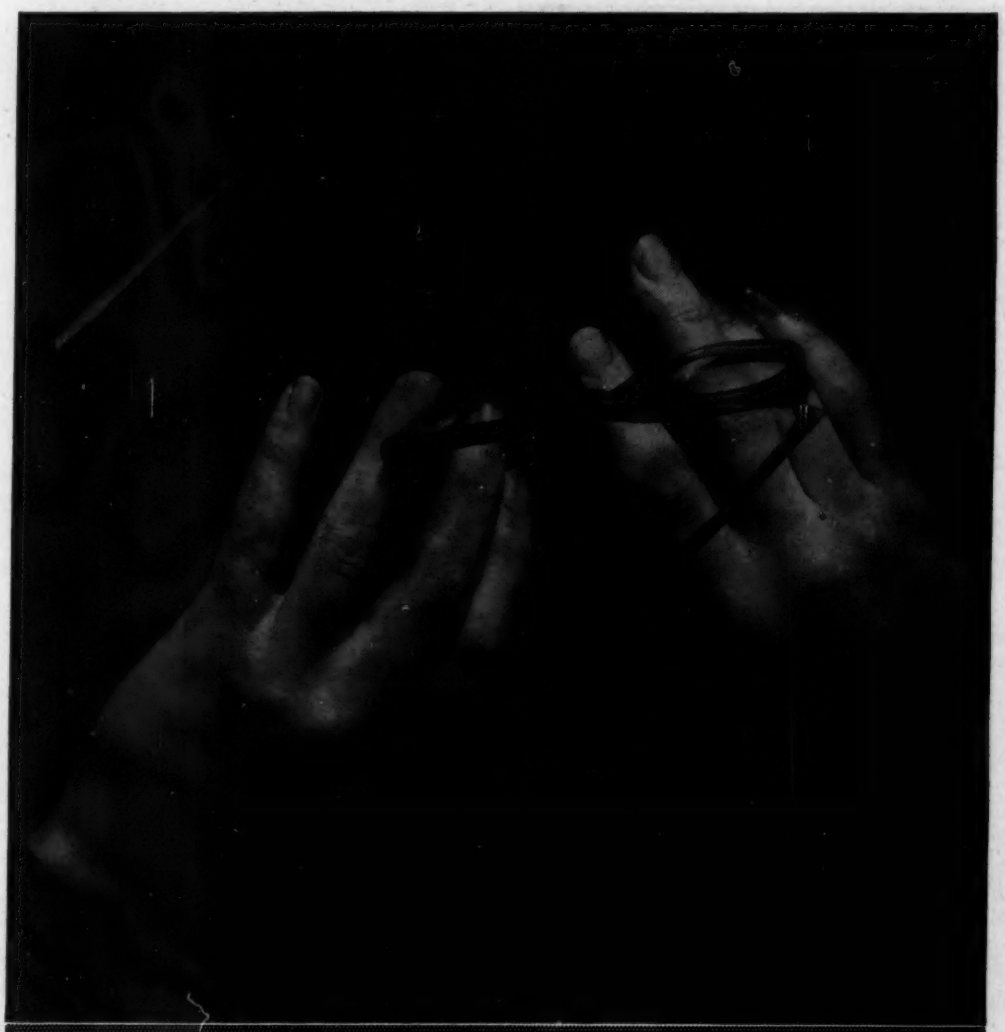

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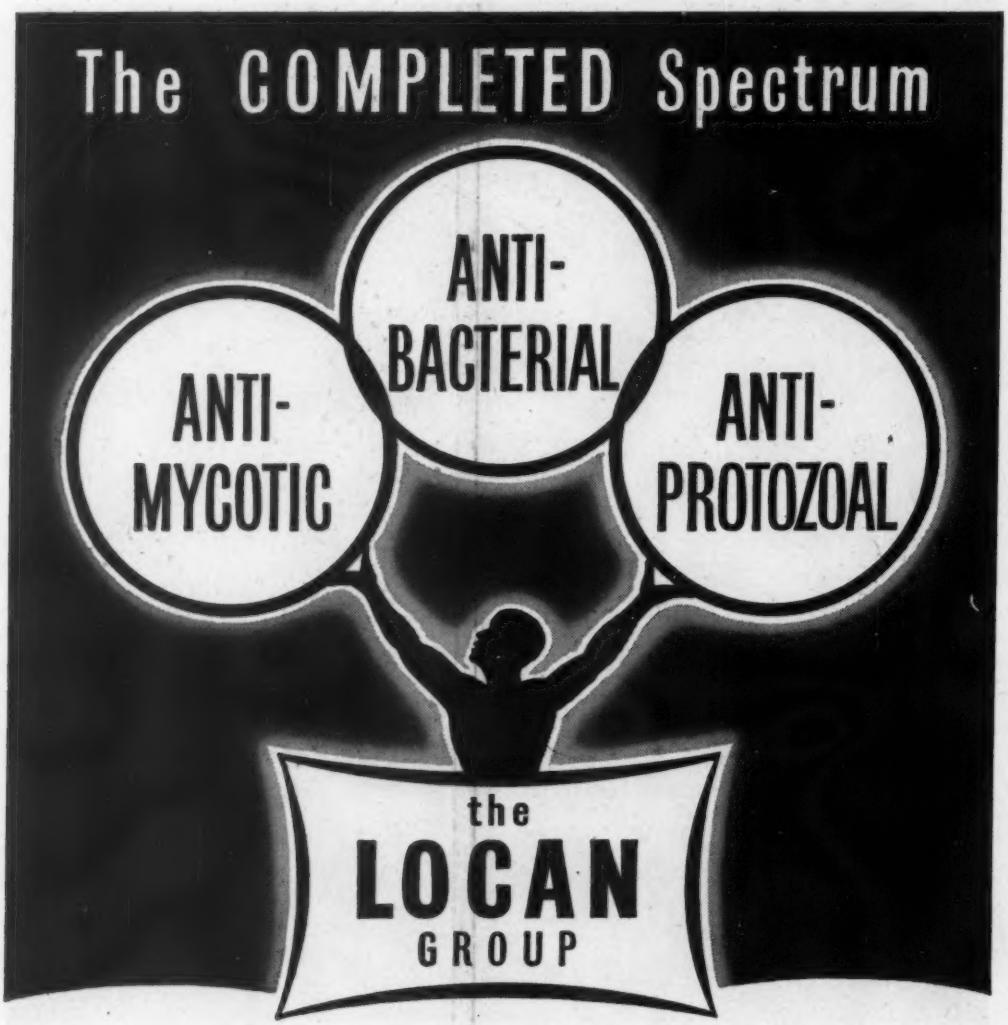

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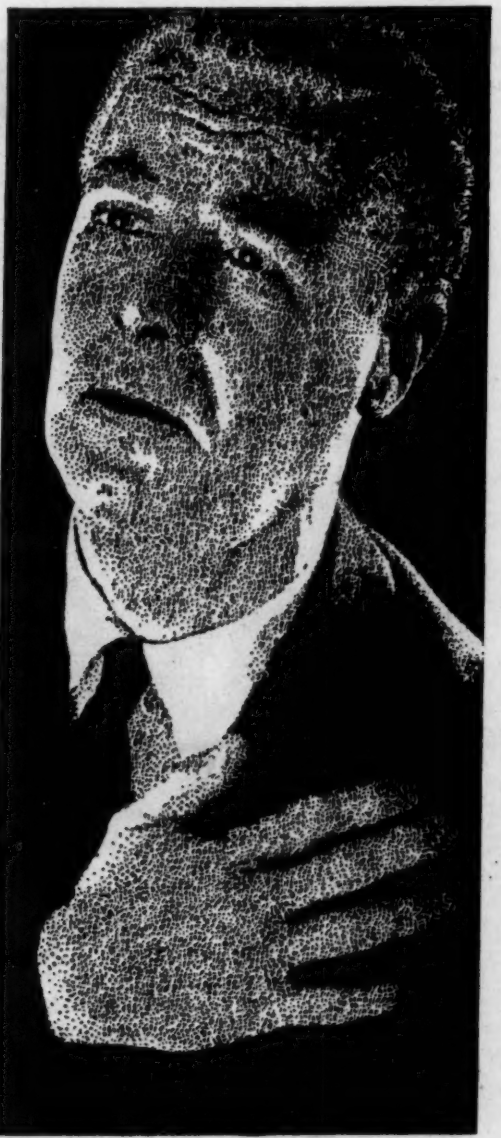

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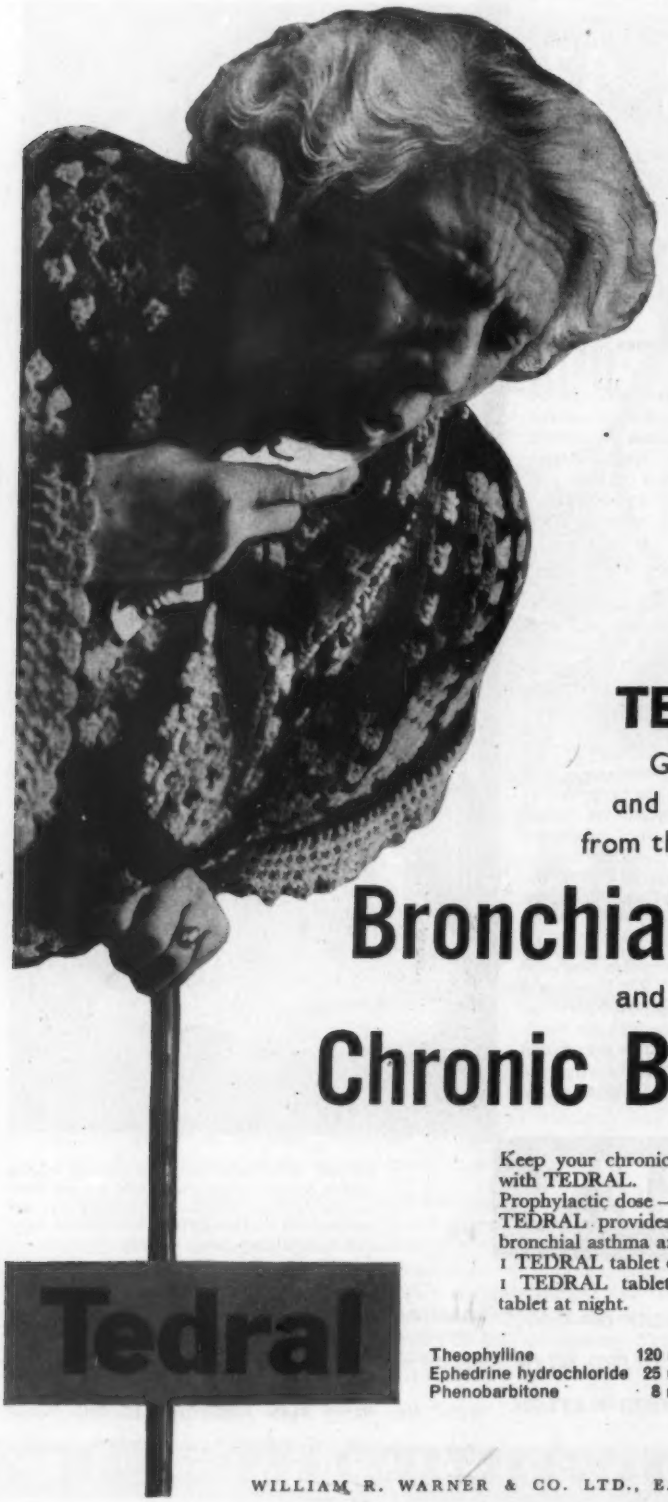

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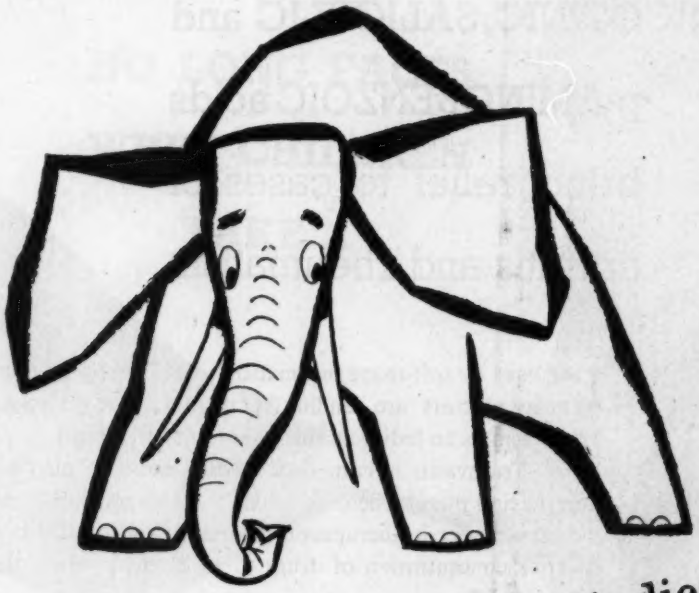

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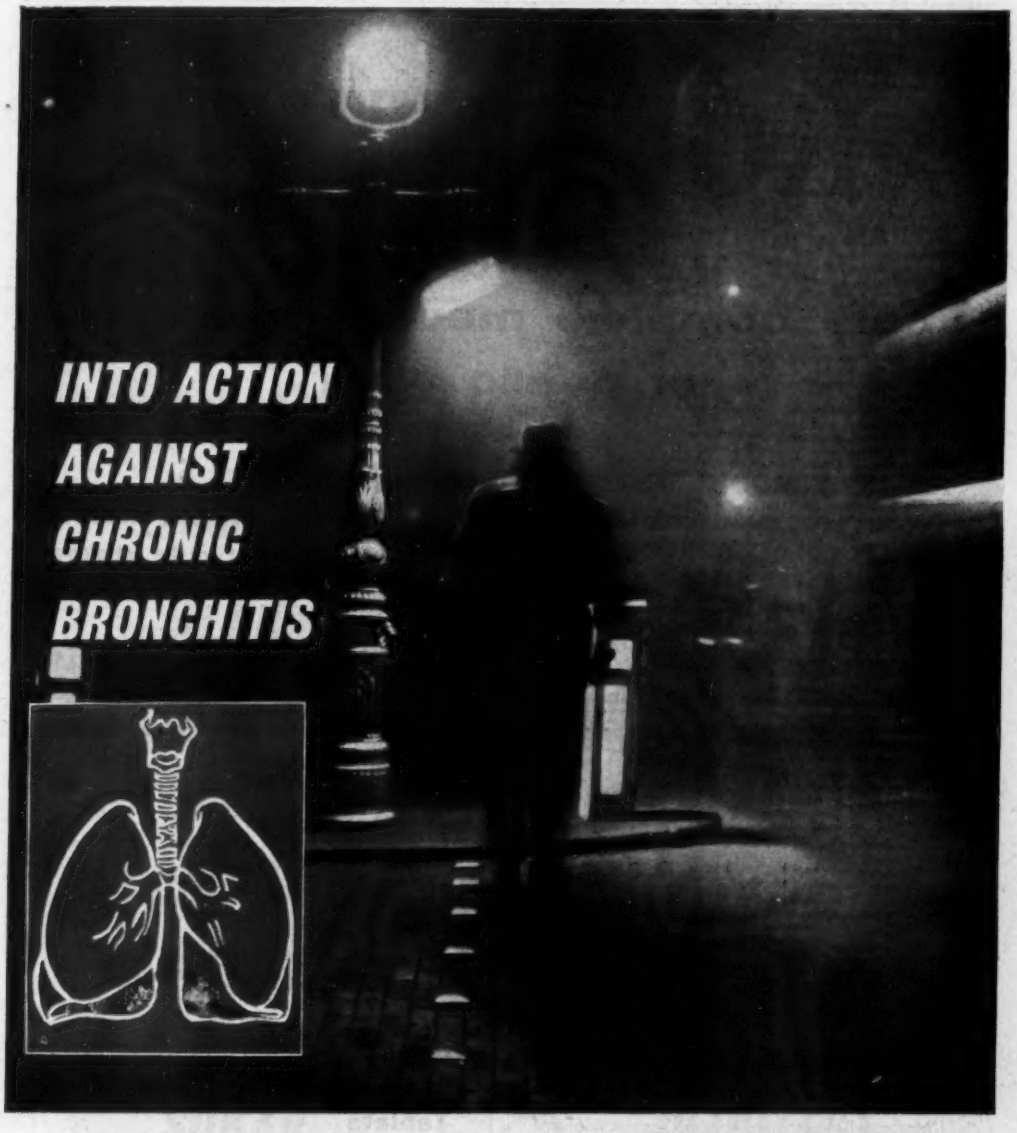

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To inhibit excess lysozyme, which is believed to be a factor in the aetiology of peptic ulcer.

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Methylcellulose	100 mg.

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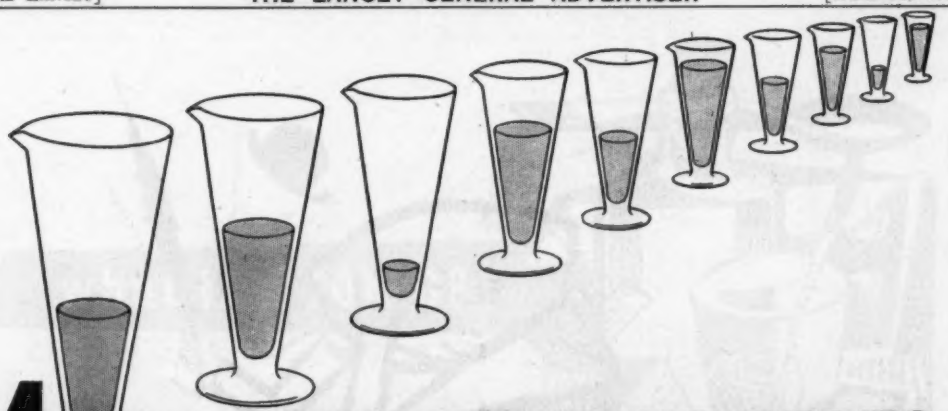

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prepared from brewers' yeast and including

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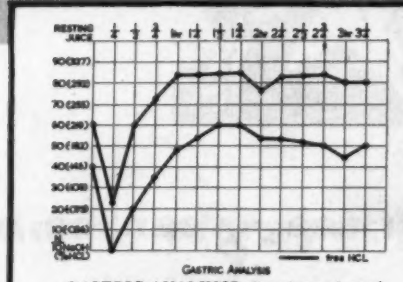
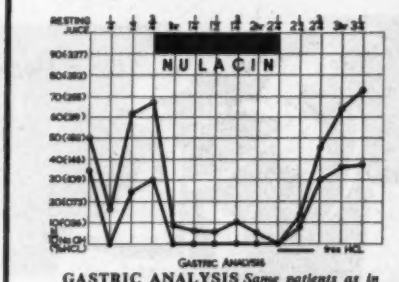


GASTRIC ANALYSIS *Superimposed gruel fractional test-meal curves of five cases of duodenal ulcer.*

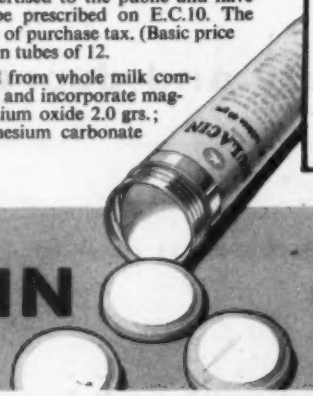


GASTRIC ANALYSIS *Same patients as in Fig. 1, two days later, showing the striking neutralizing effect of sucking Nulacin tablets (3 an hour). Note the return of acidity when Nulacin is discontinued.*

BIBLIOGRAPHY

Practitioner, 1957, **178:** 43
Practitioner, 1956, **176:** 103
Amer. J. Gastro. 1956, **26:** 665
Brit. Med. J. 1954, **1:** 46

Further references to the literature and full information on Nulacin available on request.



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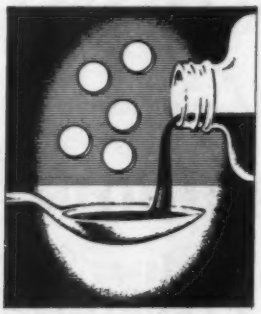

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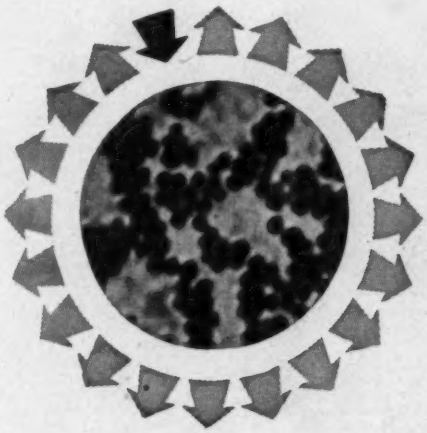

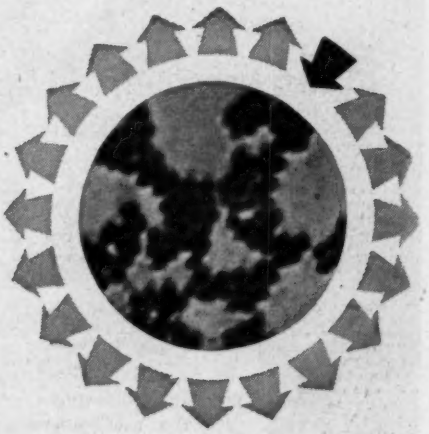

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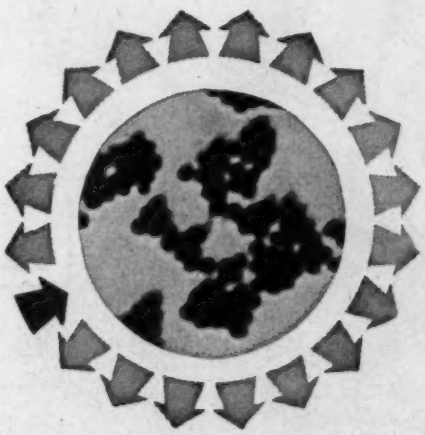

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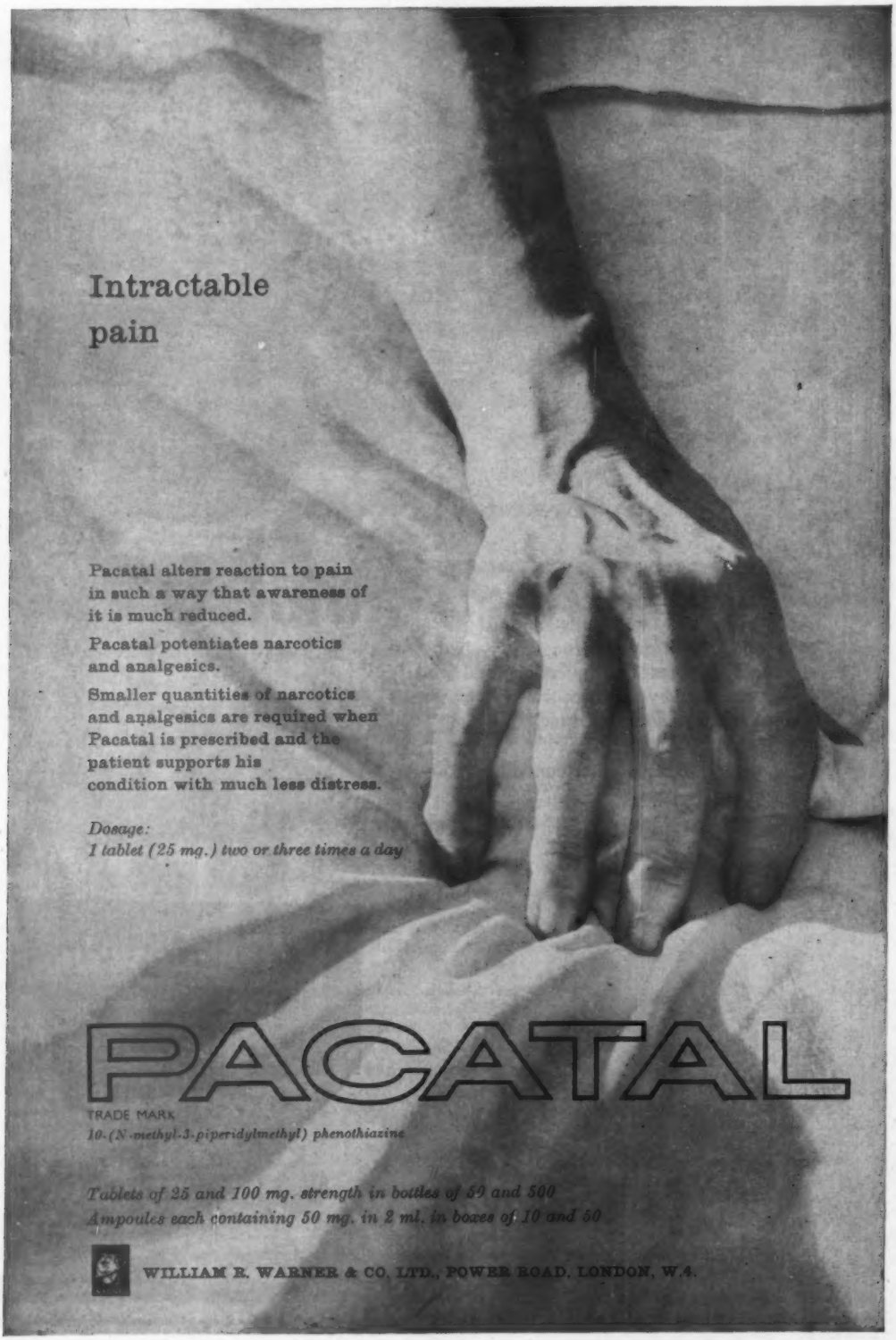
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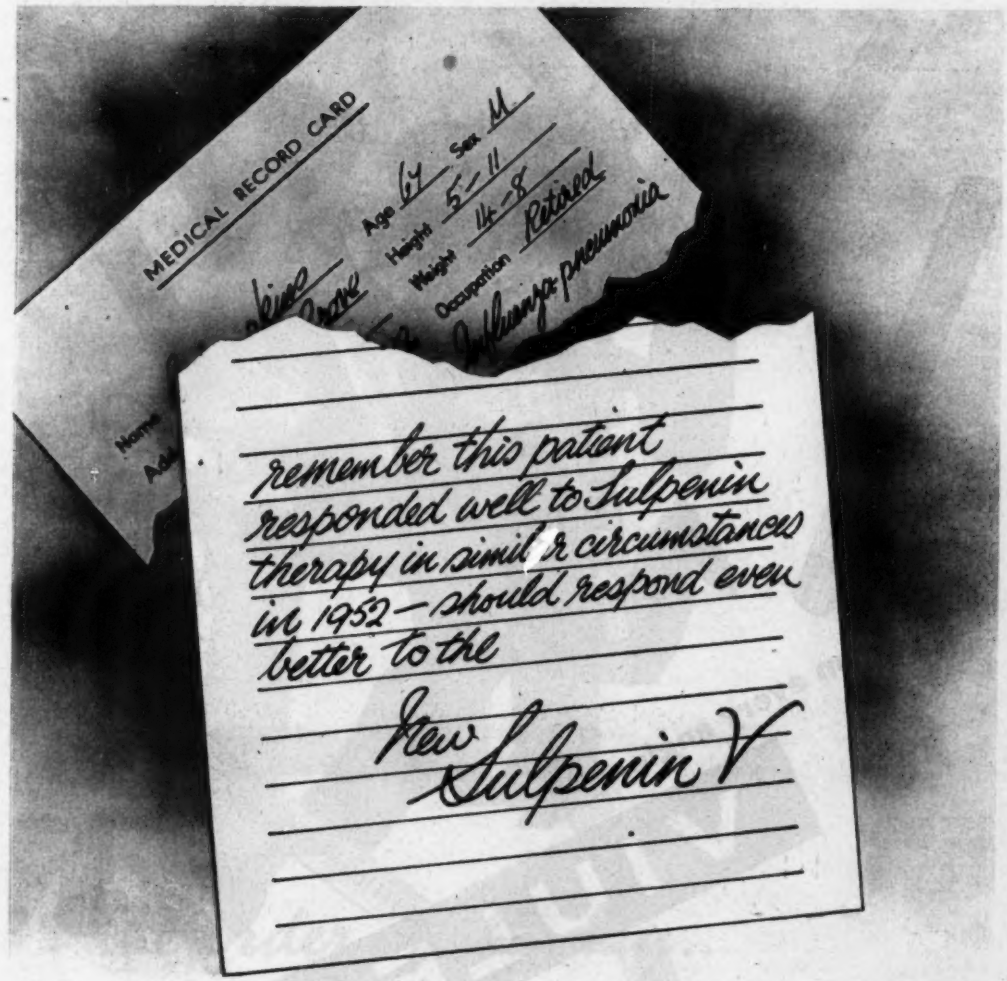
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*B.M.J. p.63, July 13, 1957.

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UNCOMMON MYOCARDIAL DISEASES

THE NON-CORONARY CARDIOMYOPATHIES*

WALLACE BRIGDEN
M.D. Cantab., F.R.C.P.

PHYSICIAN TO THE LONDON HOSPITAL AND THE CARDIAC DEPARTMENT OF THE LONDON HOSPITAL; PHYSICIAN TO THE NATIONAL HEART HOSPITAL; CONSULTANT CARDIOLOGIST TO THE SPECIAL UNIT FOR JUVENILE RHEUMATISM, CANADIAN RED CROSS MEMORIAL HOSPITAL, TAPLOW, BUCKS

THE common cause of isolated myocardial disease is coronary disease; but there are many other causes, mostly obscure and relatively rare. When patients develop apparently causeless heart-failure, diagnosis of myocarditis is sometimes made, but usually the condition is attributed either to a previous hypertension or painless coronary disease. Often such patients die unexpectedly and pathological investigation may not reveal the cause and nature of the disease. The present study is concerned with these myocardial diseases which are either isolated or so nearly isolated that disease in other systems is of a minor degree and significant only as an aid to diagnosis. The term cardiomyopathy is used here to indicate isolated non-coronary myocardial disease.

Our ignorance of myocardial diseases is reflected in a confusing terminology. Some terms, such as cardiac myopathy, cardiopathy, myocardosis, and even myocarditis are used for the whole group. Blankenhorn and Gall (1956) use the term myocarditis for inflammatory reactions and myocardosis for the rest. (Myocarditis should certainly be reserved for those conditions in which there is reasonable evidence of an infective origin.) Fiedler's myocarditis is a favourite term among clinicians: it suggests a final diagnosis but is barely more than a convenient term for cases which do not fit into any known classification. Adjectives such as isolated, idiopathic, non-specific, specific, interstitial, diffuse, and circumscribed abound in the literature; others, such as acute, subacute, chronic, pernicious, and malignant, relate to the clinical picture; while still others, such as eosinophilic, allergic, idiosyncratic, and granulomatous hint at ætiology, as does familial cardiomegaly. Endomyocardial fibrosis, fibroelastosis, fibroplastic myocarditis, idiopathic cardiac hypertrophy, and cardiomegaly relate to gross morbid anatomy. Ætiology, even if only in a broad sense, should be indicated where this can be determined and when the cause is unknown this should be stated—e.g., cardiomyopathy (unspecified).

The true incidence of these diseases is unknown but is probably higher than is generally supposed. Saphir (1941) and others have shown that histological evidence of myocarditis can often be found in the hearts of patients dying from various infectious diseases; but clearly this myocarditis is often incidental and irrelevant to the clinical problem. On the other hand, clinicians are so sensitive to the frequency of coronary and hypertensive heart-disease that they are reluctant to diagnose the non-coronary cardiomyopathies in general and myocarditis in particular. These diseases are not common; but they are more common than constrictive pericarditis, with which they are sometimes confused, and they are more common than some of the congenital anomalies which receive much attention these days.

The first part of this paper deals with some general features of cardiomyopathy and particularly with the pattern of heart-failure which often appears. The second part deals with some of the different types of cardiomyopathy on an ætiological basis.

Material

50 cases of isolated or nearly isolated heart-muscle disease (cardiomyopathy) have been investigated. All but 4 of the patients were inpatients at The London Hospital or The National Heart Hospital between 1949 and 1956. None had evidence of coronary disease, hypertension, valve disease, rheumatism, syphilis, or diphtheria. There were 2 children, aged 13 and 14, but the remainder were adults. 40 patients died, of whom 32 were examined post mortem. On the evidence of clinical history, physical examination, laboratory investigation, and necropsy, 42 of these cases could be placed into broad ætiological groups as follows:

7 presented strong evidence of familial heart-disease and were considered to be congenital.

8 appeared to be due to infection and presented the histological picture of myocarditis.

3 very similar cases occurred in late pregnancy and the early puerperium and are called "puerperal myocarditis."

3 showed features of hypersensitivity and were classified as collagen disease.

1 was associated with acromegaly.

7 showed primary cardiac amyloid disease.

13 had a long history of severe alcoholism without developing beriberi, and the condition is called "alcoholic cardiomyopathy."

It is emphasised that the common factor in this otherwise heterogeneous group of cases is the presence of serious myocardial disease without significant disease elsewhere; thus the 3 possible cases of cardiac collagen disease were not examples of one of the well-known disseminated collagen diseases.

GENERAL FEATURES

Clinical Features

Symptoms

The *onset of symptoms* in isolated heart-muscle disease is usually due to heart-failure, but occasionally the first complaint is an attack of paroxysmal tachycardia or of precordial discomfort. In the majority of cases in the present series dyspnœa on effort was the first symptom and developed insidiously; lassitude and fatigue on effort were more common than in other kinds of heart-failure. Paroxysmal dyspnœa was the first symptom in only 1 case, but isolated attacks appeared in several cases rather late in the history: it was particularly common in alcoholic cardiomyopathy, occurring in 8 of 13 patients. Most of the other patients could lie flat without breathlessness. Right hypochondrial pain on effort in a fifth of the patients and was sometimes the first symptom. A dull constant aching pain in the precordium was present in a few patients, but 3 for a time had chest pain on effort. This was indistinguishable from angina pectoris except that, in contrast to the pain of coronary disease, it started after the onset of dyspnœa. No coronary disease was found in any of the 32 cases examined at necropsy.

Palpitation was troublesome in a few patients and was due to multiple ectopic beats, paroxysmal tachycardia, or auricular fibrillation. Palpitation is especially common in alcoholic myocardial disease and occurs either with sinus rhythm or with auricular fibrillation.

Syncope or a sensation of faintness is often noted in patients with "familial cardiomegaly," occurring in 4 of 7 in this series. These patients have large hearts, often with arrhythmia, and sudden or unexpected death is a feature. Syncopal attacks occurred in 4 other patients: 1 had atrial standstill with idioventricular rhythm; 1 had a massive heart associated with acromegaly; and 2 had cardiac amyloidosis. In 1 patient syncope was related to effort, but there was no evidence of pulmonary hypertension or of other obstructive lesion.

Course.—In most patients symptoms progress quietly, but sometimes attacks of paroxysmal nocturnal dyspnœa or of paroxysmal arrhythmia make the course more rapid and stormy. Hence the signs may be maximal when the patient is first examined. But even so, apart from œdema, signs are not always obvious. The jugular venous

* The St. Cyres lecture, delivered in London on June 13, 1956.

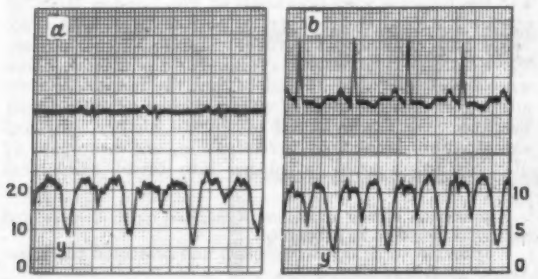


Fig. 1—Right-atrial pressure (lower register) and synchronous electrocardiograms (upper register) in (*a*) cardiomyopathy, and (*b*) constrictive pericarditis. Note high venous pressure and steep y descent in both conditions.

pressure may be so high that its upper limit is not appreciated, and the significance of triple rhythm in the presence of tachycardia in young patients is not easily assessed.

Signs

The *jugular venous pressure* is usually high (10–25 cm.). When the rhythm is regular and pressure not so high, *a* waves may be prominent. Rarely there are giant *a* waves due to the "Bernheim effect" of a massive left ventricle. The *cv* wave of tricuspid incompetence may be present, but in many patients the most conspicuous feature is a sharp *y* descent, as described by Friedreich (1864) in constrictive pericarditis, and this gives the impression of a sustained high venous pulse interrupted by a continuous downward flicking motion (fig. 1). On inspiration the level of the venous pulse may rise after a brief interval, as in constrictive pericarditis (Kussmaul 1873), and the individual waves become less conspicuous (fig. 2). Paradoxical movement of the venous pulse was observed in familial cardiomegaly, endomyocardial fibrosis, and cardiac amyloidosis. These features of the venous pulse are particularly responsible for the difficulty in differential diagnosis from constrictive pericarditis. The steep *y* descent and paradoxical venous pulse are due to the very high venous pressure and the relatively immobile heart, which are characteristic of both chronic myocardial disease and Pick's disease.

Œdema was present in various amounts in untreated heart-failure, and at first it usually cleared quickly on treatment. Pleural effusion was common. The liver was grossly enlarged in all patients in heart-failure and tended to remain so after treatment: it was presumably the source of right hypochondrial pain on effort, of which many complained. Pulmonary congestion was not usually conspicuous, and acute pulmonary œdema never developed.

The *arterial pulse* was small in the majority, mostly regular and never paradoxical, even when there was a paradoxical venous pulse. The pulse pressure was small in all cases with congestive failure, the diastolic being raised to 100 or slightly more, and the systolic ranging from 120 to 110. Peripheral constriction and other evidence of a low cardiac output was often observed. There was never any sign of systemic hypertension or of cardiovascular hypertrophy, and no patient had a hyperkinetic circulation or peripheral vasodilatation such as is occasionally found in Oriental beriberi and in hepatic cirrhosis.

The *apex-beat* was barely palpable in a few patients; in others it was of a left ventricular type, but never heaving as in hypertensive hypertrophy. In some, ventricular systole was followed by a visible or palpable diastolic filling wave coincident with the third heart sound.

Heart sounds.—The first heart sound was either soft or normal; it was never loud. The second sounds were normal in intensity but sometimes widely separated when there was bundle-branch block. Triple rhythm from the addition of the third heart sound developed in every patient in heart-failure and was often the loudest sound in the cycle; it was not so early or so sharp as the diastolic sound of constrictive pericarditis. The third heart sound tended to remain after apparently successful treatment of heart-failure. The addition of an auricular sound sometimes produced quadruple rhythm or a summation gallop. Apical systolic murmurs were heard in half of the cases; these were mostly soft, pansystolic, and variable owing to functional atrioventricular-valve incompetence. In 2 cases, where the murmur was loud, thickening of the mitral cusps was found in association with patchy endocardial fibrosis. No diastolic murmurs were heard. In many of the patients phonocardiograms were taken and confirmed the auscultatory findings.

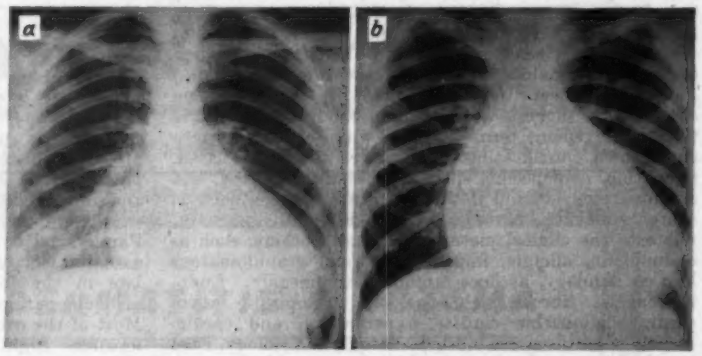


Fig. 3—Cardiomyopathy showing cardiac enlargement with clear outline of heart due to diminished movement. Minimal hilar congestion and clear lungs: *a*, puerperal myocarditis; *b*, chronic myocarditis after streptococcal infection.

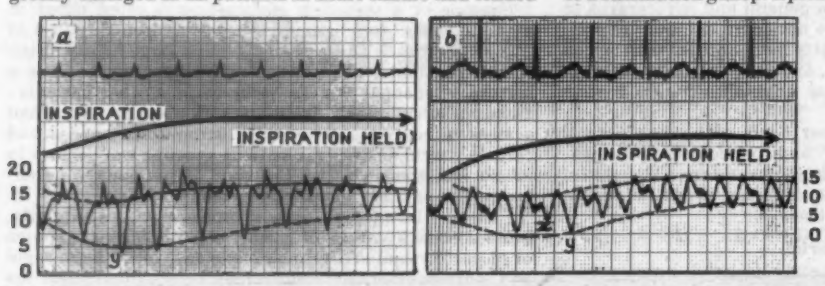


Fig. 2—Right-atrial pressure (lower register) during deep inspiration in (*a*) amyloid cardiomyopathy, and (*b*) constrictive pericarditis. After a brief initial fall the pressure rises with held inspiration in both conditions (Kussmaul effect). In amyloid cardiopathy y descents diminish, and irregularity due to A-V dissociation appears. In constrictive pericarditis *x* and *y* descents become equal as y descent becomes less.

Other systems.—A full physical examination of other systems is most important in suspected cardiomyopathy. Except in 4 cases of amyloidosis and 1 of acromegaly, however, no abnormal signs were found outside the vascular system, apart from those produced by episodes of thrombo-embolism. Nutrition was generally good, including patients with a history of alcoholism.

Death.—Sudden and unexpected death is not uncommon in cardiomyopathy. It occurs both in acute and in chronic myocarditis and in familial cardiomegaly but apparently not in amyloidosis or in alcoholic heart-disease. It is certainly untrue, in the case of cardiomyopathy, to say that "the heart is what the heart can do", for there are many recorded cases showing extensive and often chronic pathological changes in the myocardium of a patient whose physical activity was normal until he suddenly died.

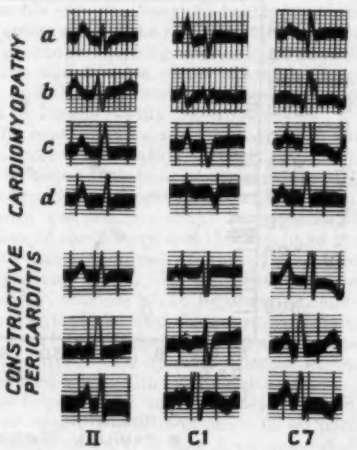


Fig. 4—Electrocardiograms (lead II and right and left chest leads) showing prominent right-atrial P waves (first component of P in leads II and C1) in cardiomyopathy: *a*, myocarditis, *b*, familial cardiomegaly, *c*, puerperal myocarditis, *d*, amyloidosis; and prominent left-atrial P waves (second component in leads II and C7) in 3 cases of constrictive pericarditis.

Radiology

Cardiac enlargement is usual in cardiomyopathy (fig. 3). Mass radiography has revealed many asymptomatic cases. The cardiac outline is "stencilled" in cases where radioscopy shows a greatly diminished movement. The right auricle is often prominent, but usually there is evidence that all the chambers are enlarged. The *pericardium* is never calcified. The *aorta* often appears small and is sometimes thought to be hypoplastic, but its apparent smallness may be due to the relatively large size of the heart. The *pulmonary artery* is usually not prominent. Hilar congestion is variable: it is often absent or slight, and this is impressive in relation to the size of the heart and the presence of congestive failure.

Other radiological appearances.—Pulmonary œdema was not seen, but small pleural effusions were common, the right side being affected more often than the left. In constrictive pericarditis the heart is relatively immobile, as in cardiomyopathy, but usually smaller; calcification is present in at least 70% of cases, and the left auricle may be selectively enlarged (Evans and Jackson 1952). As a cause of radiological enlargement pericardial effusion may if necessary be excluded by cardiac catheterisation (carried out in 7 cases).

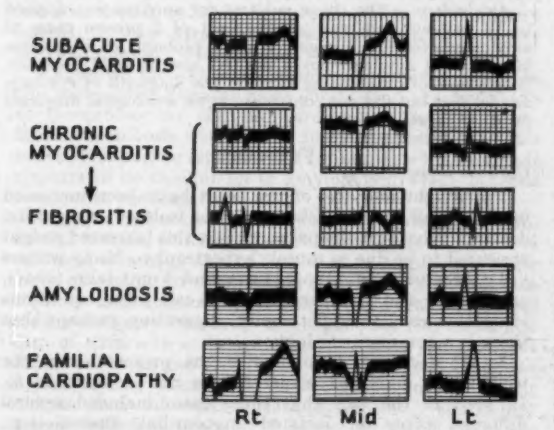


Fig. 5—Electrocardiograms (right, middle, and left chest leads) showing large Q waves, like those seen in cardiac infarction, in 5 cases of cardiomyopathy where necropsy showed healthy coronary arteries.

Electrocardiography

The electrocardiogram is always abnormal. The pathological changes are seen in many leads, indicating a diffuse abnormality rather than a local one, and in this respect there is a contrast with the usual electrocardiogram of cardiac infarction. Certain general trends may be observed in cardiomyopathy irrespective of the ætiology.

P Wave

The atrial wave was abnormal in more than two-thirds of the electrocardiograms of 35 patients in sinus rhythm (fig. 4), and the majority of these showed right-atrial preponderance, which is seen as an augmented first deflection of the P wave in right chest leads; in a few cases this change was so great that the right-atrial P wave continued to preponderate over the left, even in left chest leads. A few cases show dominant left-atrial P waves (4 cases in this series), as in constrictive pericarditis and mitral stenosis, but in these particular cases there was no doubt of the diagnosis of cardiomyopathy. Augmented right-atrial P waves may reach the height found in congenital pulmonary stenosis and may return to normal, with prolonged recovery from the heart-failure. The P-R interval was variable; it was occasionally prolonged in patients with very large hearts.

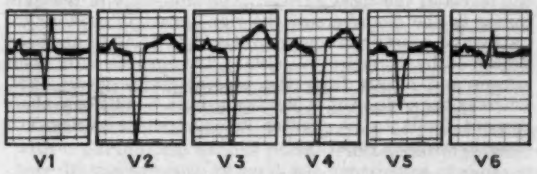


Fig. 6—Electrocardiogram of boy, aged 13, with endomyocardial fibrosis: anterior chest leads show extensive large Q waves.

QRS Complex

The ventricular complex showed various abnormalities ranging from isolated T-wave changes to gross intraventricular conduction defects. Left bundle-branch block is common (10 cases); it especially appears in association with the larger hearts and is probably a function of the hypertrophy of surviving muscle and the extent and site of fibrosis. Left bundle-branch block may not be due to a lesion in the bundle, for in some cases there was evidence of normal septal activity, and in others there was a transient bundle-branch block, presumably of a functional rather than structural origin. Those conditions associated with only slight hypertrophy usually show normal conduction time and often a low voltage. The slowly progressive lesions with much survival hypertrophy are associated with the most bizarre pathological electrocardiograms.

Q Waves

Pathological Q waves (fig. 5) appeared in 19 electrocardiograms from patients with various cardiomyopathies. In some cases these Q waves were restricted to one or two leads; in other cases they were more general (fig. 6). They presumably have the same significance as those found in extensive cardiac infarction and indicate relatively large areas of necrosis and repair of muscle. When the Q waves were correlated with the necropsy specimens, extensive necrosis or repair of muscle was found. Abnormal Q waves are especially common in amyloidosis.

T Waves

T waves were variable and usually pathological; as in other conditions, T-wave abnormalities appear as the earliest signs of myocardial disorder and later in the disease accord with the degree of muscle damage.

Other Abnormalities

No case showed right-ventricular preponderance or right bundle-branch block. It is not unusual to find the paradoxical combination of right-atrial preponderance in an electrocardiogram showing mainly left-ventricular changes. Multifocal ectopics and other arrhythmias are common, but many patients showed sinus rhythm throughout.

Cardiac Catheterisation

A comprehensive hæmodynamic study by cardiac catheterisation is contraindicated in most patients with cardiomyopathy. The risks are high when there is a large heart, frequent multifocal ectopic beats, left bundle-branch block, and large Q waves in the electrocardiogram. However, catheterisation limited to the right atrium is not hazardous, and may be useful if it is necessary to exclude pericardial effusion (fig. 7). In the present series a limited investigation was made in 7 patients (abandoned in 1), and a full study was made in 4; and in these the cardiac output was low (2·6–3·0 litres per minute). Mean right-atrial pressures were high, and there was a low pulse pressure in the pulmonary artery and the right ventricle. Immediately after the first low diastolic phase the pressure in the right ventricle rapidly attained a diastolic plateau, as in constrictive pericarditis. The wedged pulmonary arterial pressures were raised to mean levels of 20–25 mm. Hg, which were slightly higher than the levels in the right auricle. The similarity of pressure pulses in the chambers of the right heart in cardiomyopathy and constrictive pericarditis (figs. 1 and 2) has been described by Hetzel et al. (1953), but inspection of their curves and others from the present series shows that, whereas the *y* descent is similar in both conditions, the *x* descent tends to be greater in constrictive pericarditis than in cardiomyopathy.

Other Investigations

Many patients underwent comprehensive laboratory investigation. But, with the exception of biopsy in the case of primary amyloidosis, the information obtained was almost entirely negative or without known value.

Blood-counts.—No patient was seriously anæmic. Only 2 patients had definitely abnormal leucocyte-counts, although there was a tendency to find large cell types in the lymphocyte

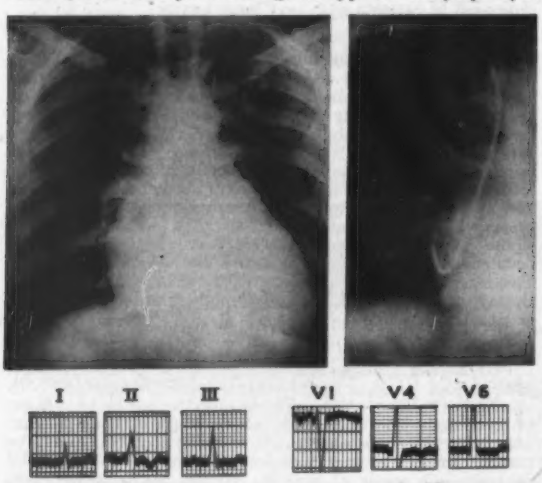


Fig. 7—Alcoholic cardiomyopathy in man aged 41: moderate cardiac enlargement; catheter in right atrium shows no effusion; electrocardiogram shows small inverted T waves (tremor in limb leads).

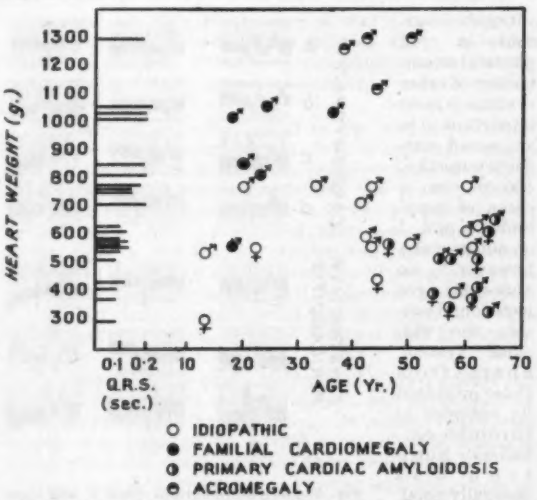


Fig. 8—Weight of heart in relation to type of lesion and patient's age. Duration of QRS on electrocardiogram shown by length of horizontal lines indicates a relationship to weight of heart at necropsy.

series. 2 brothers from a family with other cases of cardiomyopathy had a leucocytosis of 18,000–30,000 per c.mm.

Lupus-erythematosus cells were sought and not found in 6 idiopathic cases!

The *erythrocyte-sedimentation rate* (E.S.R.) was usually below 10 mm. in one hour in most of the patients; low figures were attributed to heart-failure; in those showing higher values a secondary and incidental inflammatory lesion—e.g., bronchitis and pleural effusion—seemed to be an adequate explanation.

Liver-function tests showed slight abnormalities in a few patients and did not appear to have special significance. The albumin-globulin ratio was reversed in 5 cases, and this was attributed to non-specific hepatic damage; but this change is seen more often in conditions such as amyloidosis, sarcoidosis, and hæmochromatosis, where the liver may be involved by the underlying disease.

Bacteriological investigations were negative.

Serological tests were not helpful. The Wassermann reaction was negative in all. A few patients were tested for Q fever, psittacosis, and the influenza viruses; none were found positive. Evidence of toxoplasmosis was sought in 7 cases of idiopathic cardiomyopathy; the complement-fixation test and the dye tests were negative in all, except that the dye test, which is of little specific value, was positive in a titre of 1 : 16 in 1 alcoholic patient.

Amyloidosis.—The congo-red test for amyloid was applied to 12 patients and was positive in 1 of 2 proven cases of amyloidosis tested. A negative test is probably of little value in excluding amyloid, but a positive test is good evidence. Biopsy was of outstanding value in the diagnosis of systemic amyloidosis but did not contribute to an ætiological diagnosis in other cases.

Pathology

Cardiac Hypertrophy

The weight and size of the heart have been increased in almost all the published cases of isolated myocardial disease. Whatever the pathogenesis, this increased weight appeared to be due to muscle hypertrophy. Many writers—e.g., Elster et al. (1955), Levy and Von Glahn (1944), and Serbin and Chojnacki (1955)—call these conditions idiopathic cardiac hypertrophy, suggesting perhaps that there is a common ætiology.

In 32 necropsy specimens in the present series the weight was increased (exact figures not recorded in 5). In view of the fact that these cases included several different types of isolated myocardial disease—e.g., amyloid, chronic fibrosis, idiopathic myocarditis, and familial cardiomegaly—it appears that the hypertrophy is a non-specific response of the surviving muscle to

normal hæmodynamics (fig. 8). Amyloid hearts show the smallest weight increase among the cardiomyopathies and rarely reach 650 g., most weighing 400–600 g. Hearts showing myocarditis and fibrosis of an unknown cause weigh 550–800 g., and those of familial cardiomegaly, of the type described by Evans (1949), 700–1000 g.

The weight of the heart may be roughly related to the type of lesion, but there is no relation to adult age. As it is impossible to determine the date of onset of myocardial disease (except in familial cardiomegaly, which presumably starts in utero) no relation could be established between the duration of the disease and the weight of the heart. Nevertheless one is tempted to regard length of survival as an important factor. In conditions with a relatively short history, such as acute myocarditis, subacute myocarditis, amyloidosis, and disseminated lupus, the weight of the heart is not greatly increased in the presence of extensive myocardial disease, whereas where the patient has survived a long time it weighs more.

Because extreme hypertrophy of the heart is found occasionally in acromegaly, where it appears to be part of the general splanchnomegaly, it has been suggested that idiopathic myocardial hypertrophy may have a humoral or endocrine basis. In a case of acromegaly with heart-disease, included in this study for comparative purposes, the heart weighed 1300 g. although there was no evidence of previous hypertension. From the literature it appears that heart weights are often of this order in acromegaly and well above the range found in isolated cardiomyopathies. Furthermore, none of the isolated cases in this series showed any clinical evidence of endocrinopathy or any abnormality of the pituitary gland where this was examined at necropsy. Since endocrine disease is unlikely to be a cause of the hypertrophy, and hypertension and valve disease are excluded, a non-specific survival hypertrophy remains the most probable explanation.

Myocardial Lesions

The pathological processes of inflammation, necrosis, repair, and hypertrophy tend to affect all parts of the myocardium but are often more easily recognised in the larger muscle mass of the left ventricle. However, in occasional cases the walls of one chamber may be almost exclusively affected—e.g., in a woman, aged 48, who died of a Stokes-Adams attack, microscopy showed almost no surviving normal atrial tissue ; and in a young man who died suddenly the right ventricle was almost exclusively damaged. The subendocardial region of the myocardium seems to be particularly vulnerable in all forms of cardiomyopathy. Dominant fibrosis of the endomyocardium has been seen in collagen disease, idiopathic inflammatory lesions, in the African disease, and even in primary amyloid disease.

Almost all the published reports of morbid anatomy in the myocardial diseases have emphasised the frequency of thrombosis on the endocardium of the ventricles. Mural thrombosis was seen at 20 of 32 necropsies in this series ; it occurs in all types of cardiomyopathy, though it appears to be uncommon in amyloidosis (where it tends to occur in the auricles).

Organisation of clot probably leads to patches of endocardial fibrosis, which may show unevenly as an increased opalescence among the trabeculæ or as large thick white areas extending over several centimetres. It is possible that repeated endocardial clotting, with organisation and confluence, may be partly responsible for the occasional case of extensive endocardial fibrosis observed in Great Britain. Davies and Ball (1955) have suggested that such a process may be a factor in the pathogenesis of their African cases of endomyocardial fibrosis. Ventricular mural clotting is probably followed by rapid shrinkage and organisation. It is possibly a recurring process which, once it is established, leads to progressive deterioration through further interference with myocardial nutrition.

Systemic and pulmonary embolism occurs in the cardiomyopathies, but the mural thrombi must be fairly firm because in this series there were only 2 clinical episodes of thrombo-embolism, although mural thrombosis was so often found at necropsy.

Differential Diagnosis

Constrictive pericarditis and pericardial effusion, coronary-artery disease, and hypertensive heart-disease with or without the Bernheim syndrome occur commonly among the incorrect diagnoses in cases of proven cardiomyopathy.

Pericardial Disease

Patients with cardiomyopathy may appear to have constrictive pericarditis, because of the quiet insidious development of right heart-failure associated with a very high jugular venous pressure which rises paradoxically with held inspiration. Furthermore, a sound in early diastole occurs in both conditions. The filling sound of constrictive pericarditis occurs earlier and is rather higher pitched than the third sound which occurs in muscle disease.

Radiography usually shows a smaller heart in constrictive pericarditis, but in some cardiomyopathies, particularly amyloidosis, the heart is only slightly enlarged. In amyloidosis, however, there are sometimes other manifestations of systemic infiltration, and the electrocardiogram is always different from that of constrictive pericarditis. Calcification of the pericardium is decisive, but its absence in 30% of cases of Pick's disease increases the difficulty.

The electrocardiogram in cardiomyopathy usually shows prominent right-auricular P waves, whereas left-auricular P waves preponderate in constrictive pericarditis. Pathological Q waves do not occur in constrictive pericarditis ; nor does left bundle-branch block, whereas both are common in heart-muscle disease.

The rare cardiomyopathy presenting insidious failure with a paradoxical venous pulse, a left-atrial preponderance in the presence of mild left-ventricular changes on the electrocardiogram, and with a small heart on radiography is the really difficult problem. Only 1 such case occurred in 50 cases of cardiomyopathy. Cardiac catheterisation may help, but it appears that a final diagnosis in such cases must be made by pericardiotomy because of the possibility of surgical treatment for pericardial constriction.

Patients with constrictive pericarditis often feel better and look less sick than those with cardiomyopathy.

Coronary-artery Disease

The occasional case of coronary disease developing quiet heart-failure may be difficult to differentiate from cardiomyopathy, but the episodic history of coronary disease, with the emphasis on pain, and an electrocardiogram showing relatively localised changes are usually pathognomonic. It must be emphasised, however, that precordial pain is not uncommon in the cardiomyopathies, and that cardiac infarction may be painless. Acute idiopathic myocarditis may present like an acute cardiac infarction (Gillis and Walters 1954). Right-atrial P waves are not usually prominent in coronary disease as in some cardiomyopathies, but Q waves are commonly found in both conditions and are the basis of real difficulty in differential diagnosis. Coronary disease is so common that it is perhaps diagnosed too readily.

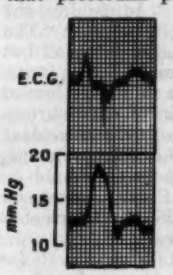


Fig. 9.—Electrocardiogram and right-atrial pressure in child with cardiomyopathy showing massive left ventricle at necropsy. V1 shows tall P waves, and right-atrial pulse shows giant *a* waves with no *y* descent.

Hypertensive Heart-disease

Patients with myocardial disease are not infrequently diagnosed as having "fallen hypertension," particularly when the diastolic pressure may be a little high from peripheral constriction in heart-failure. Some pathologists are especially likely to diagnose hypertensive heart-disease when a heavy heart is discovered at necropsy; but, when the signs of cardiovascular hypertrophy from hypertension are sought and not found, and when histological examination is completed this error is unlikely to remain. In 2 cases in this series the macroscopic diagnosis at necropsy was hypertensive heart-disease, although no hypertension, vascular hypertrophy, or renal disease had been noted during several years' clinical observation.

Bernheim's Syndrome

Hypertension or aortic-valve disease associated with gross left-ventricular hypertrophy does not present serious difficulties in differential diagnosis. In some cardiomyopathies, however, there is gross left-ventricular hypertrophy, and then the Bernheim effect may cause large *a* waves and contributes to the picture of right heart-failure without dyspnœa. In 1 child with cardiomyopathy proven at necropsy hypertrophy and bulging of the intraventricular septum was so great that giant *a* waves and large P waves in the electrocardiogram led to the erroneous diagnosis of tricuspid stenosis (fig. 9).

(*To be concluded*)

TUBERCULOUS CERVICAL ADENITIS

T. J. WILMOT
M.S. Lond., F.R.C.S.
CONSULTANT EAR, NOSE, AND THROAT SURGEON TO COUNTIES TYRONE AND FERMANAGH

E. F. JAMES
M.D. Belf., M.R.C.P.I.
CONSULTING CHEST PHYSICIAN TO COUNTIES TYRONE AND FERMANAGH

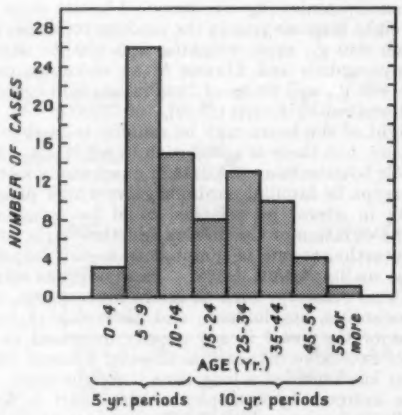
L. V. REILLY
M.D. Belf., B.Sc., D.P.H.
CONSULTING CLINICAL PATHOLOGIST TO THE NORTHERN IRELAND TUBERCULOSIS AUTHORITY

SCROFULA was being treated by the "Royal Touch" as early as the 5th century, and by surgery in the 17th century (Guthrie 1945); yet the treatment of tuberculous cervical adenitis, as Lester (1951) points out, is still controversial. Surgeons vary in their therapeutic advice from block dissection to simple aspiration, and the discovery of the potent antituberculous drugs may have encouraged physicians to believe that surgical treatment should be applied only when conservative treatment has failed. The pathogenesis is no less controversial. To some adenitis is merely the local manifestation of a general disease, to others the result of an isolated primary infection of tonsil, adenoid, or even teeth. "In children the bacilli are usually of the bovine type" (Boyd 1944). "The human type of tubercle bacillus is responsible for all but an occasional case of lymph node disease" (Lester 1951).

It was in the hope of deciding on a definitive line of treatment that the present investigation was started. We also hoped to assess the importance of coincident tuberculous infection in the tonsils and adenoid tissue, and to decide whether this lymphoid tissue should be removed, and, if so, at what stage. Finally, it seemed possible that we might help to reconcile the various conceptions of the ætiology and pathogenesis.

The Patients

This report is based on 81 cases of tuberculous cervical adenitis in Counties Tyrone and Fermanagh, referred to ear, nose, and throat or chest clinics between November, 1951, and July, 1956. The condition is not uncommon in this area; 26 new cases were seen in 1954 and the same number in 1955. In 1956 the figure had fallen to 15 (a 40% reduction on 1954 and 1955) but it was still sufficient to merit attention. The vast majority of these patients have had involvement of the upper deep cervical lymph-glands, and in the 60 cases in which this group of glands has been involved the infection has been unilateral in all but 2—that is, in 97%.



Age-incidence of patients when first seen.

All patients needing surgical treatment have been admitted, under one of us (T. J. W.) at the Tyrone County Hospital, Omagh, the most central hospital in the area, where cooperation between surgeon and chest physician has enabled surgery and chemotherapy to be closely integrated. All tuberculous material has been examined bacteriologically by one of us (L. V. R.), and all histological work has been under the supervision of Dr. J. E. Morison, consulting pathologist to the Central Laboratory, Belfast.

Age-incidence

Cervical adenitis is regarded as chiefly a disease of children (Boyd 1944, Price 1956), and certainly the maximum incidence in our series was in the 5th to 9th year (see figure). But 37 of our 81 patients (46%) were over the age of 15, and 29 of these (36%) were over 25. Thus any study which is confined to children must necessarily miss many cases. None of our patients were under the age of 3, although pyogenic cervical adenitis is common below this age.

History and Symptoms

In only 8 cases had glands been enlarged for less than a month before the patient came for treatment, and, at the other extreme, in 8 they had been noticed for ten years and over. In 57 cases the lump had been noticed for between one month and three years. A patient's account of the length of time a swelling has been present is often unreliable, since a stationary swelling can remain unnoticed, and we found that it was usually progressive enlargement which drew attention to the lesion. This was the most common reason for seeking medical advice, because constitutional symptoms, pain, or tenderness were almost always absent.

Glands Affected

In 71 cases only *one* gland group was affected. Of these, the deep cervical chain (usually jugulodigastric gland) was involved in 60, the submandibular group in 5, the posterior-triangle group in 3, the supraclavicular group in 2, and the facial group in 1. In 10 cases more gland groups than one were affected—the deep cervical chain and submandibular groups in 5, the deep cervical chain and posterior-triangle group in 3, the deep cervical chain and supraclavicular triangle group in 1, and the submandibular group and facial gland in 1.

Other Tuberculous Lesions

In 4 of our cases (5%) active pulmonary tuberculosis accompanied the cervical adenitis. (The glands affected were the deep cervical chain in 2 cases, the supraclavicular group in 1, and both the deep cervical chain and the supraclavicular group in 1.) In 1 case a pulmonary lesion had healed before the glandular neck disease began. 17 patients (21%) gave a history of previous tuberculosis, and in 12 of these the previous lesion had been a cervical adenitis. A long latent period was sometimes a feature. Thus a woman, aged 42, who presented herself with a cold abscess in the left side of her neck in 1955, had had a similar abscess on the right side twenty-three years before. Another woman gave a history of cervical adenitis twenty-eight years previously. In 95% of our patients, however, the glandular lesion was the only manifestation of active tuberculosis while they were under our care.

Bacteriology

Extrapulmonary tuberculosis is customarily associated with bovine infection (Aird 1957, Barrington-Ward 1952), and in some countries such infection may be prevalent.

Wissler (1954) says that 80% of cases of cervical adenitis in Swiss children are caused by the bovine bacillus, but provides little bacteriological evidence for this statement. The members of the American Trudeau Society's Committee on therapy (1954) believe that cervical-gland tuberculosis is more often human than bovine in origin, and Rich (1951) said: "In the majority of cases of cervical adenitis in which the bacillus has been typed the human type bacillus has been found."

The bovine tubercle bacillus, however, is not a common cause of extrapulmonary tuberculosis of any kind in Northern Ireland (Reilly 1950), and we believe that the human bacillus was responsible for most of the lesions in the present series.

Our bacteriological investigation included examination of pus aspirated from glands or cold abscesses before operation, examination of tissue from excised glands, and in some cases examination of tonsil and adenoid tissue.

Cultures were made from all the samples of pus and caseous material for secondary organisms, but in no case were any isolated. Samples were obtained from 54 cases, and in 41 of these (76%) typical tubercle bacilli were demonstrated by direct smear examination. Fragments of tissue were, when necessary, emulsified in a Griffith's tube with 5% potassium hydroxide. The tissue or pus was inoculated on Löwenstein-Jensen and on Dorset egg medium (without glycerin), and was also inoculated into guineapigs in all cases. The culture and inoculation were repeated in some cases where more than one specimen was available. It was possible to isolate living tubercle bacilli in only 4 cases; in 3 they were human and in 1 bovine. The bovine case was confirmed by rabbit inoculation.

We had hoped to obtain some evidence of the incidence of bovine organisms in this cervical gland material, which was derived almost entirely from patients living in country districts; but the investigation was very disappointing in this respect. A sister of the 1 patient with proven bovine infection also had tuberculous cervical adenitis, and it might be presumed that she too was infected with a bovine strain.

The difficulty of recovering living organisms from cervical glands is well known. In one investigation (Medical Research Council 1949) it was impossible to recover tubercle bacilli by culture or animal inoculation from 81·3% of cervical glands. Soltys (1953) has shown that a bacteriostatic substance is present in tuberculous glands in animals, and that saline extracts of the tissue will inhibit the growth of a culture of living tubercle bacilli.

In the experience of one of us (L. V. R.) the recovery of organisms is not so difficult in the occasional case in an elderly person, or where cervical glands are only part of a more general infection. Perhaps the relative innocuousness of localised cervical-gland lesions is partly due to some process in the gland which leads to the death of the infecting organism.

Latterly, it has seldom been possible to isolate a bovine strain in more than 1 case each year from all the material coming to the central laboratory of the Northern Ireland Tuberculosis Authority, and this includes organisms from pulmonary, osseous, genitourinary, miliary, meningeal, and glandular lesions. The few bovine strains isolated have been mainly from patients whose disease was contracted several years ago. The sale of milk is now strictly controlled; about 95% of the milk produced is pasteurised; and the number of attested herds is increasing steadily. The bottle of milk is now a common sight outside the country cottage, even in remote districts.

Circumstantial evidence of human infection is the fact that a family history of pulmonary tuberculosis was found in 10 cases (12%). If 5 cases are added in which healed or active pulmonary lesions were present as well as the cervical adenitis, a total of 15 cases (19%) is obtained in which the human tubercle bacillus almost certainly caused the glandular disease. Pulmonary tuberculosis is very rarely caused by bovine infection in Northern Ireland, and it is unlikely that different lesions in the same person or in the same family would be caused by different types of tubercle bacillus. Further indirect evidence was the discovery of positive or suggestive radiological signs of healed primary tuberculosis in the lungs in 38 of the 81 cases.

Ætiology

The involvement of lymph-glands is essentially a feature of primary tuberculosis, but our experience suggests that, though cervical adenitis is part of an original primary infection, the infection need not have been recent. Of 167 home contacts, only 1 person was found to have active pulmonary tuberculosis. There was a family history of pulmonary tuberculosis in 9 other cases, but in all of these the history was remote. It is notoriously difficult to persuade all members of families to present themselves for examination, but our investigation of contacts, particularly those of the children, was as complete as we could make it.

Evidence of Healed Primary Lesions in the Lungs

All but 6 of our cases were X-rayed, and we were impressed by the large proportion of films showing what seemed to be evidence of healed primary lesions in the lungs. Since this evidence is difficult to assess, we submitted all films to Dr. J. W. Winchester, consulting radiologist to the Tyrone County Hospital. Of the 75 films he examined, 38 (51%) showed obvious or suggestive evidence of healed primary tuberculous lesions in the lungs; but since the primary complex in the lungs can subside without leaving any radiological trace, it is possible that more patients had had primary pulmonary lesions. Our failure, in almost all our cases, to find a recent source of tuberculous infection, coupled with the evidence of healed primary disease in so many of them, suggested to us again that the seeds of cervical adenitis are often sown far in the past.

The Pathway of Infection

The tonsil's liability to tuberculous infection is well known, and the evidence from our series tends to incriminate it. Tonsillectomy was performed in 47 cases. In 30 of these the tonsils were examined histologically, and in 14 (47%) there was evidence of tuberculosis. That the tonsils can be tuberculous without glandular involvement has been pointed out by Suzuki (1955) who was able to culture tubercle bacilli from the tonsils of 16 out of 32 patients who had quiescent pulmonary disease and who needed tonsillectomy because of chronic tonsillitis. The appearance of the tonsils on clinical examination seems to be no guide to the presence or absence of tuberculous infection. The high incidence of tuberculous infection in tonsils examined histologically in our series suggests that the tonsils should always be removed when tuberculosis affects the upper deep cervical group of glands. Furthermore, recrudescence of infection in a quiescent but obviously tuberculous gland has often been associated

with attacks of non-specific tonsillitis. We have a strong impression that, when a tuberculous cervical gland has lain quiescent for many months or years, the commonest reactivating factor has been an acute tonsillitis. We think it likely, therefore, that the tonsil is the most common source of tuberculous cervical adenitis and that it is infected by inhalation at the time of the primary infection. Some of the tubercle bacilli remain in the tonsil and the remainder pass to the lungs to produce the familiar Ghon lesion with hilar adenitis. Healing would thus seem to be the rule, apart from a little caseous material in the cervical glands which remains to await a suitable stimulus for reactivation.

Histological Findings in the Tonsil

Dr. J. E. Morrison reported as follows:

Fourteen examples of tuberculosis of the pharyngeal tonsil have been seen in the three-year period in this material. Two of these were in adults aged 24 and 36 years.

It is impossible to recognise, or even to suspect, the condition on gross examination. Areas suggestive of caseation in tonsils are usually simple epithelial inclusion cysts containing epithelial debris. Histological recognition has not been difficult; in ten cases the lesions were numerous and in varying stages of evolution; in all, a distinctive follicular arrangement of large mononuclear cells was present with some follicles showing at least some caseation in all cases. Usually some follicles show multinucleate giant cells. In all, fibrosis and encapsulation was absent, and the large caseous areas often seen in lymph-glands were also absent. There was no surface ulceration. The lesions often showed spread with numerous secondary follicles, in varying stages of evolution. No study for tubercle bacilli in sections was made, but sufficient caseation was found in all to exclude Boeck's sarcoidosis, and there was no real comparison with the lesion of abortus fever.

The distribution of the lesions showed a distinctive preference for lymphoid tissue close to the surface, and to the tonsillar crypts in seven cases; this seemed consistent with an infection entering from the surface. In three cases the lesions were widespread and in four they were few, and no suggestions as to the route of entry were justified in either group. In nine of the fourteen cases adenoid tissue was also received, but only one, a woman aged 24 years, showed specific lesions; in this case the distribution in the tonsil was recognisably in relation to the surface and the tonsillar crypts; but in the remaining six cases showing this distribution, four had adenoid tissue examined with completely negative results.

If the infection is primary and airborne, and if there is a free nasal airway, it may be somewhat difficult to explain the relative immunity of the adenoids. However, on the whole, the histology is consistent with the entry through the tonsil, and is perhaps comparable to the primary lesions of the bowel where the point of entry may show relatively little pathological change while drainage lymph-glands are enlarged and caseous.

We have already referred to the remarkable difficulty in culturing tubercle bacilli from pus obtained from the lesions in our cases. Yet there was little difficulty in finding the bacilli on direct examination.

It might be argued that chemotherapy was responsible for this difficulty, for the patients were receiving anti-tuberculous drugs at the time of operation, but the failure of these drugs to penetrate caseous material is the main disadvantage of the chemotherapy of tuberculosis, and difficulty in culturing tubercle bacilli from the pus from cervical glands was noted long before the days of chemotherapy. We believe, with Denis Browne (1956) and Jones (1951), that cervical adenitis and abscess formation are common because the mouth, throat, and nasopharynx are so vulnerable to recurrent pyogenic infection. The Shwartzman phenomenon (Rich 1951) in which the bombardment of a tuberculous focus with non-specific inflammatory stimuli evokes hæmorrhage and necrosis in the focus, could be the mechanism of the adenitis and could also explain why the tubercle bacilli in these lesions are difficult to culture. A similar mechanism has been described by Jones in his interesting paper on tuberculous lymphadenitis in the Nigerian.

Management

Once active tuberculous infection of the cervical glands is suspected, the diagnosis must be confirmed and treatment begun. Our policy is to admit all cases to hospital within a few days as semi-emergencies. A thorough general examination is then made, the chest is radiographed (and if necessary the neck), and tuberculin-sensitivity tests are done. The latter are of considerable diagnostic significance; in 50 recorded and proved cases, 31 were positive in a dilution of 1/10,000 and 13 in a dilution of 1/1000; only 1 was negative. Once the diagnosis has been confirmed or is strongly suspected, chemotherapy is started, and it continues throughout surgical treatment and for a total period of not less than three months.

Where the disease is bilateral and is evident well down the neck, extension from the mediastinum should be suspected. Chemotherapy, prolonged if necessary for many months, is then the treatment of choice, and surgery should be limited to aspiration or curettage of cold abscesses, though limited surgical excisions may be possible later. In 76 of our 81 cases (94%), however, the infection was unilateral, being localised to one or more glands of the upper group. In 60 patients (74%), only the upper deep cervical group of glands was affected, and our treatment of this, the main group, is basically excisive surgery for all uncomplicated cases not responding rapidly to simpler measures. Calcified glands should not be excised; but a partially calcified gland, guilty of frequent flare-ups, should be excised if the patient is young.

Once surgical treatment has been completed, the patient is sent home and continues his chemotherapy under the direction of his general practitioner.

Surgical Principles and Technique

If there is softening or frank abscess formation, surgery is directed first towards the glands, because delay makes excision more difficult and is likely to lead to more skin involvement with consequent scarring. If there is no evidence of softening, surgery is directed first towards the tonsil and adenoid tissue or towards eliminating dental sepsis. Whether any of these structures is infected with tubercle bacilli or pyogenic cocci is immaterial; the risk of infection ought to be removed. These simple procedures alone will be sufficient to allow many glands, at first thought to be tuberculous, to resolve without further treatment. In such cases, the tuberculin skin reactions are usually negative.

If the gland does not quickly lessen in size after tonsillectomy, the patient can be sent home on chemotherapy. If it increases in size, or shows any tendency to break down, it should be excised without delay. Among our 40 cases where the clinical diagnosis of tuberculous adenitis was not in doubt, there were no fewer than 33 (83%) in which surgical excision proved necessary because tonsillectomy and chemotherapy did not clear up the adenitis. Hence, when everything indicates an isolated gland infection, there is much to be said for following up the tonsillectomy by a routine dissection of the gland. We did this increasingly often as our series continued, and we think it important to excise glands before a cold abscess forms and skin is involved.

As soon as the diagnosis is confirmed we give isoniazid (5 mg. per kg. body-weight) with P.A.S. (1·5 g. for each 50 mg. tablet of isoniazid). In very young children isoniazid syrup is given and the P.A.S. omitted. But chemotherapy though useful in conjunction with surgery, has seldom been effective by itself; and this is in keeping with the mechanical difficulty in getting the agents into the avascular tissue affected.

It is often possible to excise a cold abscess and underlying gland in one mass. If the overlying skin is involved, but not extensively, it should be sacrificed; such involve-

ment should not be allowed to delay surgical excision, but on the contrary should spur the surgeon to early action. If much skin is involved, preliminary aspiration or curettage, with prolonged chemotherapy, may be necessary to reduce the lesion to satisfactory surgical dimensions. Here, experience is the best guide. In dissection of the skin over a cold abscess, the use of fine plastic surgery skin-hooks is helpful. Careful, gentle, anatomical, sharp dissection of the whole lesion should be carried out, and suction should be available to remove any spilled tuberculous pus. The key to most of these dissections is the sternomastoid muscle; once this has been carefully defined from the surrounding (and often dense) fibrous tissue, other landmarks become plain. Gentle retraction and the use of fine plain catgut, rather than diathermy, facilitate healing, which is usually very rapid. Incisions are, of course, placed in the line of the skin creases, and the least possible skin is excised. All obviously tuberculous glands should be removed, but normal glands should be left in situ.

With long-continued chemotherapy, a diffuse tuberculous mass is often reduced to a more localised lesion which can be excised. Sometimes, however, a cold abscess is so extensive or in such a position as to preclude excision. In these circumstances we open the area widely, using a skin-crease incision, and under direct vision curette both the abscess and the gland responsible for it. The incision is then stitched carefully, allowing room for a small drain and a polyethylene tube through which the cavity may be irrigated with P.A.S. solution.

Any residual gland tissue can if necessary be excised later. In the few cases where we have used this method there has been no secondary infection.

All wound cavities, before suture, have been irrigated with P.A.S. solution. In spite of the spilling of tuberculous pus and tedious, lengthy dissections, all our wounds have healed by first intention. There is little or no postoperative pain and a minimum of painful ward dressings. There is no doubt in the minds of most of the patients that they suffer more after tonsillectomy than after the neck dissections.

Results

Of those patients deemed suitable for surgery, glands were excised in 54.

Simpler methods, such as aspiration and incision with curettage, were used in only 11 cases; in 6 of these glands were excised later. No skin-grafts have been necessary.

Of the excised glands, 51 were upper deep cervical, 8 were submandibular, 1 was submental, and 1 was facial.

The results of excision have clinically and cosmetically been good. In all but 3 of the patients operated on, the cervical lesion seems to have cleared up completely. In the 3 in which enlarged glands recurred deep to the cervical scar, a further simple excision and continuation of chemotherapy have resulted in apparent cure.

We have not found it necessary to treat these patients with the protracted rest and other general measures often advocated; once the cervical lesion has been excised, convalescence need not be long, and we return children to school within two or three weeks of the operation. Many patients have been home on the fifth day, and the average for all cases operated on has been between seven and eight days. Because of poor rural communications, many have had to stay longer than was strictly necessary.

Operative Complications

Nerve injuries.—The spinal accessory nerve was divided in 1 case where a large mass of glands had been present for two years had and not responded to chemotherapy. The nerve was traced into and out of the mass but could not be freed. It was divided. In this case, full function has returned to the affected muscle.

In 3 patients, the cervical branch of the facial nerve was cut; in only 1 of these is any weakness of the angle of the mouth now visible.

Keloid has formed in only 2 patients, and then only to a minor degree. Both have received radiation therapy with benefit.

Summary

A series of 81 cases of tuberculous cervical adenitis is described. In 54 cases the glands were excised and in 47 the tonsils were removed. To date 3 patients have relapsed; relapses were treated also by excision without further relapse.

In 95% of our cases the disease was limited to the cervical glands and treatment of the local lesion resulted in cure. Protracted rest is unnecessary.

The treatment of choice is surgical excision. Chemotherapy, however, is useful to "cover" the operation period, to prevent relapse, and to reduce periadenitis before operation.

Surgical treatment includes routine removal of oral and pharyngeal sepsis, with particular attention to dental caries and tonsillectomy.

Tonsillectomy should be done *before* surgical excision of the glands if there is no evidence of gland softening or cold-abscess formation—and *after* excision of the gland when softening is present.

The human tubercle bacillus seems to have been responsible for most of these lesions, which, it is argued, represent the recrudescence of old tuberculous foci and not recent infections.

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LONG-CONTINUED TREATMENT WITH TETRACYCLINE AND PREDNISOLONE IN CHRONIC BRONCHITIS

A CONTROLLED TRIAL

E. N. MOYES
M.D. Edin., M.R.C.P.E.
CHEST PHYSICIAN

R. A. KERSHAW*
M.B. Manc., M.R.C.P.E.
ASSISTANT CHEST PHYSICIAN

ROYAL INFIRMARY, WORCESTER

ORAL antibiotics provide a ready means of suppressing at least temporarily the *Hæmophilus influenzæ* and the pneumococcus, which have been shown by many workers, including Mulder et al. (1952), May (1953a and b, 1954), and Stuart-Harris et al. (1953), to be responsible for the infected sputum and acute exacerbations in chronic bronchitis.

In the early case the prompt and vigorous antibiotic treatment of each and every chest illness may halt the pathological processes so well described by Reid (1954) and spare some patients from serious disability. In the advanced case, however, the most that can be expected of this treatment is a slowing down of the progressive lung changes by preventing the deterioration which so often follows each acute attack. In these circumstances long-continued chemotherapy may be more successful than the intermittent treatment of acute exacerbations. May and Oswald (1956), who gave tetracycline or oxytetracycline

*Dr. Kershaw died on Aug. 3, 1957.

through the winter months to 37 advanced bronchitics noted striking improvement in 22 of them in terms of the amount and purulence of the sputum, acute illness, absence from work, and general well-being. In 14 of these patients observations made during a previous winter were used as a control in the assessment of results. With even longer treatment the experience of Helm et al. (1954, 1956) in 17 cases was equally encouraging, but the trial was uncontrolled.

In the assessment of any new therapy in chronic bronchitis, difficulties abound, for objective measurements are few and some reliance must be placed on the patients' impressions, which are notoriously biased by expectation of success and by the wish to please the doctor who is trying to help. We have therefore attempted a blind controlled trial of the clinical value of long-continued chemotherapy, and we have also taken the opportunity to study the effect of corticosteroid hormones given in conjunction with antibiotics.

For the purposes of this trial, chronic bronchitis was defined as a chronic condition of at least two years' duration, characterised by a productive cough throughout the year and normally associated with dyspnœa and bronchospasm.

Preference was given to patients with pus in their sputum, and only those with moderate or severe disability were accepted. Care was taken to eliminate patients with typical bronchial asthma and with the so-called asthma-bronchitis or infected asthma, where differentiation between the two conditions is difficult, one merging into the other as infection supersedes on an asthmatic basis. Also excluded were patients with past or present evidence of cardiac failure, significant hypertension, peptic ulceration, or mental instability, who might have responded unfavourably to steroid therapy. Selection was not influenced by the coexistence of healed tuberculosis, pneumoconiosis without progressive massive fibrosis, slight bronchiectasis, limited pulmonary fibrosis, or emphysema.

Materials and Methods

All patients with chronic bronchitis attending the chest clinic between Nov. 5, 1956, and Jan. 10, 1957, were assessed as regards their suitability for inclusion. 81 males and 9 females, aged 20–67 (average 53), were admitted to the trial. In 4 of them productive cough was confined to the winter months, but in other respects they satisfied the criteria of selection.

Trial Groups

By a random allocation system supplied by the Medical Research Council the patients were divided into three treatment groups, A, B, and C. Except where toxic reactions or acute illness demanded a break of secrecy, the individual allocations were known only to the clinic sister, who was also responsible for the distribution of trial substances.

The original plan was to use the double blind method with only two groups, changing from control to trial substances or vice versa at the halfway stage. However, despite its obvious advantages, this method had to be discarded in view of the Medical Research Council report on chronic asthma (1956) which suggested that the early benefits of steroid therapy gradually decreased after the first eight weeks. As only the winter months are available for experiment in chronic bronchitis, it thus became necessary to give the treatment continuously throughout the trial period and to use an untreated control group.

Treatment

The duration of the trial was four months in each case, and during this time continuous outpatient treatment was given as follows:

Group A (control).—Dummy tablets 2 t.d.s. for seven days, then 1 t.d.s. Aminophylline 0·1 mg. t.d.s.

Group B.—Tetracycline 500 mg. t.d.s. for seven days, reduced thereafter to 250 mg. t.d.s. Aminophylline as in group A.

Group C.—Tetracycline as in group B: Prednisolone 5 mg. t.d.s.

The dummy tablets were orange in colour and indistinguishable from those of tetracycline. The aminophylline and prednisolone, referred to as the white tablets, were similar in appearance.

Tetracycline was chosen for its known efficacy against *H. influenzæ* and the pneumococcus and preferred to oxytetracycline because it is said to be less likely to cause toxic symptoms. The dosage was calculated to be heavy enough to control infection in most of the cases without undue side-effects. However, from previous experience with tetracycline in this dosage in outpatients, troublesome diarrhœa was anticipated in some cases; so to mitigate this nuisance, each patient was warned that this symptom might occur. If it did so, as expected, in the first week, he was told to reduce the daily dose of orange tablets from 2 to 1 thrice daily and to inform his doctor or the chest clinic of his trouble. Neither vitamin supplements nor nystatin tablets were given as a routine; the latter were given if a simple kaolin mixture failed to control diarrhœa.

The prescription of other antispasmodics and medicaments in tablet form was discouraged. All patients were taught breathing exercises, which they practised with varying enthusiasm.

Assessment

At entry to the trial, and at monthly intervals, observations were made on the following:

(1) The daily volume and purulence of the sputum graded as mucus (0), mucopus (+), or pus (++).

(2) The number and severity of head colds and acute exacerbations and the number of days ill or off work.

(3) The degree of dyspnœa determined by Fletcher's (1952) questions.

(4) The degree of bronchospasm, assessed by physical examination, in the grades described in the M.R.C. report on cortisone in chronic asthma (Medical Research Council 1956).

(5) Measurement of vital capacity (in 54 cases).

(6) The nature and severity of any side-effects of treatment.

(7) The patient's and the doctor's opinion of the effect of treatment on his various symptoms and well-being.

In addition each patient kept a simple daily log of his progress, and local weather was recorded during the winter months. At the start and finish of the trial patients were asked to submit three specimens of sputum for bacteriological examination by the method described by Rawlins (1953). Eosinophilic pus was never seen, although sputum from each patient was examined for it.

Results

Of the 90 patients admitted to the trial, 32 were treated with dummy tablets and aminophylline (group A), 29 with tetracycline and aminophylline (group B), and 29 with tetracycline and prednisolone (group C). Table I gives details of these groups at initial assessment by average age, duration of symptoms, daily amount and purulence of the sputum, degree of spasm and dyspnœa, and ability for work. In these and other respects the three groups were closely similar.

In 11 patients (5 in group A, 2 in group B, and 4 in group C) the group allocation was known at some stage of the trial because acute illness or toxic symptoms demanded a break of secrecy.

4 patients were withdrawn from the trial. A control in group A had a severe pneumonic illness seven days after the start, did not keep subsequent appointments, and was not traced. 2 patients (1 each in groups B and C) refused to take the prescribed treatment after they had had severe diarrhœa and abdominal pains within the first fortnight. The 4th patient (in group B) developed an acute duodenal ulcer soon after the start of treatment with tetracycline and aminophylline and was not seen again.

The overall results based on serial observations made at the initial and four subsequent monthly assessments in the 86 patients remaining in the trial are presented in table II. Slight degrees of improvement and deteriora-

TABLE I—COMPARISON OF TREATMENT GROUPS

Group	Average age (yr.)	Average duration of bronchitis (yr.)	Average daily sputum (oz.)	Purulence of of sputum			Bronchospasm (grades)			Dyspnœa (grades)					Unable to work
				0	+	++	1	2	3	1	2	3	4	5	
A (32 cases) ..	54	11	2	5	23	4	5	15	12	..	2	19	9	2	13
B (29 cases) ..	52	17	2	6	22	1	3	11	15	..	7	12	8	2	8
C (29 cases) ..	53	16	2	4	20	5	4	11	14	1	6	10	10	2	12

tion have been included in the "unchanged" category; "better" and "worse" signify a change in either direction of considerable or moderate degree. It will be seen that more than half the patients in groups B and C obtained significant benefit compared with only 2 (6%) in group A. (In this group 5 patients shown in table II as "unchanged" claimed moderate improvement; but usually the patients' and the doctors' opinions agreed closely.) The results in groups B and C are remarkably similar and strongly suggest that the improvement was due to the long-continued treatment with tetracycline and not to the prednisolone, which on this analysis appears to have no greater effect than aminophylline.

Sputum

Perhaps the most dramatic effect of antibiotic treatment was reduction in the twenty-four-hour volume and in the purulence of the sputum, usually within the first two weeks. The daily volume was reduced by at least 1/8 oz. and often to negligible proportions in 44 (80%) of the 55 patients who received tetracycline whereas only 11 (35%) of the control group noticed any improvement. 46 of the former originally had pus in their sputum as judged by naked eye. Conversion to mucoid was observed in 32 (69%) (25 by the fourth week and 7 others by the eighth week of treatment): in the control group the conversion-rate was 30%. There was no significant difference between the results in the two treatment groups. It should be appreciated that our assessment takes account only of the sputum samples inspected during follow-up visits, and conversion therefore only implies a general trend. Several patients had a recurrence of infected sputum during exacerbations between visits, but this has been ignored.

5 patients in group A and 10 in groups B and C started the trial with mucoid sputum. In 2 of the former, pus was present on subsequent examinations, whereas in the treated groups the mucoid character persisted in every case and 3 claimed significant benefit. Usually it was noted that, as the sputum diminished, cough was relieved; but this was not invariable, and several patients, mostly in the treatment groups, reported as much distress from the effort to produce small quantities of sticky mucus.

Bacteriology

No special provisions were made for bacteriological examination of the sputum samples, which were dealt with as part of the routine work of a busy laboratory. Most were sent by post, when the interval between production and examination of the samples was sometimes as long as three days. The low yield of potentially pathogenic organisms was undoubtedly influenced by these two factors; for *H. influenzæ* was isolated from purulent sputum in only 19 cases, and the pneumococcus in 8. The commonest organism was *Staphylococcus pyogenes*, which was cultured in 38 cases. In 5 patients the same organisms, sensitive in vitro to tetracycline, were isolated in pre-treatment sputum and at the completion of therapy: *Staph. pyogenes* in 2, and *H. influenzæ* in the others. In 3 of these cases good clinical results were obtained; indeed the presence or absence of pathogenic bacteria in pre-treatment sputum did not appear to have any prognostic significance.

TABLE II—OVERALL EFFECT OF TREATMENT

Group	Better	Unchanged	Worse
A (31 cases)	2	26	3
B (27 cases)	16	9	2
C (28 cases)	17	10	1

Exacerbations

An attempt was made to classify episodes of symptomatic deterioration as mild, moderate, or severe, with a range from slight aggravation due to inclement or changing weather conditions to the opposite extreme of pneumonic illness. However, so varied were these episodes in their effects on different patients that consistent classification was impossible, and in the final analysis they were described as either "severe" or "less severe." A severe exacerbation denotes an acute chest illness associated with febrile symptoms, retiral to bed, and at least five days' total incapacity. Table III illustrates the occurrence of such incidents in each treatment group.

TABLE III—NUMBER OF EXACERBATIONS AND OTHER TREATMENT GIVEN

Group	Free from exacerbation	Exacerbations		Other treatment	
		Severe	Less severe	Antibiotic	Symptomatic
A (31 cases)	2	15	53	17	13
B (27 cases)	2	6	46	5	6
C (28 cases)	7	7	32	2	9

The patients in group C appeared to fare better than those in group B in relation to the total number of exacerbations, the difference being due to the larger number who had a trouble-free winter. Both treatment groups showed an advantage over the controls, particularly in the reduced number of severe episodes. This is reflected in the prescription of other antibiotics seventeen times in the control group, five times in group B, and only twice in group C.

A direct comparison between the number of exacerbations during the trial and those during the same months of the previous winter was not attempted, because of big differences in weather and the difficulty of obtaining a reliable retrospective history. Correlation between the dates of onset of each illness and the prevailing weather does no more than confirm that bronchitics are susceptible to sudden changes of temperature and humidity and particularly tend to relapse in cold damp weather. There was no particular association with fog, which developed on thirty-eight days between November and April but was rarely dense.

There was little difference between the three groups in the average time lost from work by those patients who were initially fit for employment. 1 patient in group A, 4 in group B, and 4 in group C resumed work during the trial.

TABLE IV—EFFECT OF TREATMENT ON DYSPNŒA AND BRONCHOSPASM

Group	Dyspnœa			Bronchospasm		
	Better	Unchanged	Worse	Better	Unchanged	Worse
A (31 cases)	1	25	5	2	26	3
B (27 cases)	11	14	2	11	13	3
C (28 cases)	9	17	2	14	11	3

Many bronchitics have a continuous watery nasal discharge during the winter or throughout the year, and others tend to have more head colds than other people. 52 patients in this series gave a history of persistent nasal catarrh, but only 27 were troubled with this complaint during the trial. Abnormally good weather was probably responsible for much of this apparent improvement. There was no evidence that steroid treatment offered any benefit, although there was a greater reduction in the incidence of this complaint in the two treatment groups than among the controls.

Other Symptoms

Table iv illustrates the effect of the three therapeutic regimes on dyspnœa and bronchospasm. Usually worse in the early mornings and fluctuating with the degree of bronchial obstruction by secretions, œdema, and bronchospasm, dyspnœa is difficult to assess independently in bronchitics. Here only a rough measurement was attempted by questioning the patient about his exercise tolerance at each interview, sustained improvement in grade being recorded as "better," "worse" signifying the opposite, and "unchanged" the remainder. The same categories were used to describe bronchospasm, graded by the patient's own observations and the auscultatory findings at each examination. The results in the treatment groups were significantly better than obtained in the controls and closely mirror the overall results. Simple vital-capacity recordings at monthly intervals in 54 patients did not yield any additional information. This benefit seemed to be derived from the suppression of infection; and prednisolone, in the dosage used, seemed to be no better than aminophylline at any stage of the trial.

Side-effects

Apart from the 2 patients withdrawn from the trial because of diarrhœa, this side-effect was reported by 33 (60%) of the 55 patients who received tetracycline, with a similar proportion affected in groups B and C.

In 19 it was mild, but in the other 14 it was severe enough to call for modification of treatment. In 5 patients the tetracycline was stopped temporarily until the symptom abated; in 3 a reduction in dosage for a week or two sufficed. 4 patients were never again able to tolerate more than 0·5 g. b.d., and in 2 other patients long-continued treatment with another antibiotic (oxytetracycline 750 mg. daily in one and sigmamycin 750 mg. daily in the other) was substituted after efforts to reintroduce tetracycline had failed.

With 1 exception diarrhœa began in the first week of treatment, when the patients were receiving tetracycline 1·5 g. daily. Normally it cleared within seven to ten days without specific treatment (nystatin was used on five occasions), but in some cases frequent loose stools were experienced for several weeks after the initial acute attack. Stomatitis was noted twice.

It was feared that this high incidence of diarrhœa might invalidate the blind nature of the trial by indicating when tetracycline and not the dummy substance was in use. However, this fear was largely unfounded, because of the remarkable occurrence of diarrhœa in 12 (39%) of the controls. In 5 cases this amounted only to frequent and poorly formed stools for the first few days; but the others claimed frank diarrhœa, which in 2 cases required the temporary cessation of treatment. Such action was also taken in a further control, who had severe abdominal pains in the first fortnight; but these may have been due to aminophylline, which was stopped at the same time.

Throughout the trial a close watch was kept for side-effects of steroid therapy, and the dosage of prednisolone was reduced or stopped at the first sign of possible toxic symptoms. In several cases the steroid was probably innocent; but, rather than court disaster, treatment was modified.

Thus it was stopped permanently in a man who developed congestive failure at the end of the third month, and reduced to 7·5 or 10·0 mg. daily in 7 patients for various reasons, including hypertension, excessive weight gain, slight moon-face, vasomotor instability, and bouts of depression.

2 other patients had unequivocal reactions. One developed an acute depressive state on the fifteenth day from which he rapidly recovered; after an interval of nine days the steroid was reintroduced and was tolerated at 15 mg. daily for the rest of the trial. The other patient developed symptoms and signs of peptic ulceration and was tender over a deformed duodenal cap. Prednisolone was stopped for four weeks, during which his symptoms abated, and was then gradually built up to full trial dosage without event.

A further patient said that his bronchospasm was considerably aggravated by prednisolone; this was confirmed by experiment in the last month of treatment.

Discussion

An underlying difficulty of therapeutic trials in chronic bronchitis is the incompleteness of our knowledge of its causes. A precise and generally accepted definition is lacking, and there is no single criterion by which therapeutic response can be accurately assessed. The best the physician can do is to judge results in terms of symptoms and signs, all of which are subject to natural variation and difficult to measure with any accuracy. The results obtained here must be viewed in this light.

Under the conditions of a blind controlled trial, which have been outlined, long-continued tetracycline therapy benefited 33 of 55 moderately or severely disabled bronchitics to whom it was given, whereas only 2 of 31 control patients were similarly improved. Often the improvement in health and wellbeing was dramatic, being more than expected in a relatively mild winter and more than is normally obtained from symptomatic treatment with breathing exercises, antispasmodics, inhalers, vaccines, and cough medicines. With the suppression of infected sputum, symptomatic relief was usually noted within the first two or three weeks' treatment, and if it took longer than this to appear it was rarely maintained or of high degree. However, all the patients whose sputum changed from pus to mucus were not helped, some experiencing greater distress in clearing their chests of the more viscid mucoid material; wheeze and breathlessness often persisted unchanged despite progress in other respects. Fewer severe exacerbations occurred in the treated patients, but 750 mg. of tetracycline daily rarely offered complete protection from illness during the four winter months which constituted the trial period in each case. If it had been possible, as in normal practice, to vary the dosage according to individual requirements, increasing beyond the maintenance level at the first sign of symptomatic deterioration or a return of pus in the sputum, perhaps some of these episodes might have been avoided.

Long-continued chemotherapy requires the use of highly expensive oral antibiotics effective against the potential pathogens. It carries with it a possible risk to the individual and the community of the development and dissemination of antibiotic-resistant staphylococci and other organisms. Its effect as a symptomatic suppressant in any given case is unpredictable, and the extent to which the natural course of bronchitis is influenced by such therapy is not yet known. However, despite these disadvantages, it appears to be the best available treatment for some severe bronchitics at present.

The patients most likely to benefit, and in whom a trial is justified, are a small proportion of the bronchitic population—those liable to frequent exacerbations whose sputum is predominantly or frequently purulent. When the sputum is infected only during infrequent exacerbations and is otherwise mucoid, the immediate and vigorous treatment of each illness with chloramphenicol or one of the tetracyclines appears preferable to maintenance therapy. Although, ideally, pathogenic bacteria should be isolated from the sputum as a preliminary, this is probably unnecessary in practice, so long as false eosinophilic pus found in certain asthmatics is not overlooked. Such cases do not respond to long-continued chemotherapy (Helm et al. 1954, May and Oswald 1956) and were deliberately excluded from this series by taking a careful history; as a result eosinophilic pus was never seen.

In a few cases as much as 2·0 or 3·0 g. of tetracycline daily may be required to control infection, but in most cases 1·5 g. daily or less will achieve this object, and after a week or so the dose can be reduced to a maintenance level. If there has been no symptomatic relief by the third or fourth week, continuation is a waste of time and money. Success at this stage usually merits daily treatment during the winter months and occasionally throughout the year.

A serious drawback to tetracycline therapy is the liability to diarrhœa. The reported incidence of this complication in hospital series varies between nil and 15%, but it is recognised that ambulant patients are more likely to have gastro-intestinal disturbance during treatment with broad-spectrum antibiotics than are patients at rest (Waddington et al. 1954). Here diarrhœa was reported by 60% of the patients who were given tetracycline and by 39% of those who received only the placebo tablets and aminophylline. Aminophylline 0·1 g. t.d.s. may cause gastric irritation, but diarrhœa is not mentioned as a toxic symptom by Goodman and Gilman (1956); the placebo tablets containing small quantities of starch and lactose must be judged innocent. Thus the only rational explanation of these high figures, particularly in the controls, lies in the effect of suggestion on the lower alimentary tract, consequent on a warning which each patient was given of the possibility of developing diarrhœa. If diarrhœa can be caused in this way, it is interesting to reflect as a corollary how greatly faith and encouragement can bias patients in favour of a new remedy.

Some observers favour allergy as the dominant ætiological factor, believing that infection plays but a small and incidental part. Although there are many arguments for this hypothesis, which claims a fundamental similarity between asthma and bronchitis, it has not had the attention it deserves—mainly because physicians, on the whole, have been more impressed by the need to differentiate the two conditions from the therapeutic viewpoint (Oswald 1954). Measures which control asthma rarely succeed in the chronic bronchitic, and vice versa. The results of steroid therapy obtained in this trial illustrate this difference in therapeutic response. Prednisolone in a maintenance dosage usually effective in bronchial asthma (5 mg. t.d.s.) was added to the antibiotic regimen in 28 patients, and the results were compared with those obtained in 27 patients on aminophylline (0·1 g. t.d.s.) and tetracycline. The relief of bronchospasm and dyspnœa, reduction in the amount and purulence of sputum, and overall improvement were similar in the two groups. Prednisolone did not influence the persistent nasal catarrh, which is a common symptom in bronchitics, but it was associated with a slight reduction in the total number of exacerbations.

These findings suggest that corticosteroids have little if any value as maintenance therapy in established bronchitis, but they do not justify an opinion on the efficacy of corticosteroids given in large dosage to hospital inpatients actutely ill with bronchitis. In such cases Ogilvie and Newell (1957) are enthusiastic about the value of corticotrophin combined with appropriate antibiotics, but contrary opinions, which our personal experience supports, have been expressed by Felix-Davies and Westlake (1956) and others. This controversial problem, and the place of steroids in the treatment of so-called infected asthma or asthma-bronchitis, require further investigation.

Summary

90 cases of moderate or severe chronic bronchitis were included in a blind controlled trial to assess the value of outpatient treatment with long-continued daily tetracycline, with and without prednisolone, during four months of the 1956–57 winter. The results obtained in 86 patients, divided into three treatment groups, are described.

Significant and often dramatic improvement was observed in 60% of the patients in the two groups who received tetracycline. This compares with 6% improvement in the group where dummy tablets were substituted for the antibiotic. The standard maintenance dose was 250 mg. t.d.s., with 500 mg. t.d.s. for the first week. Diarrhœa was reported in 60% and in 25% was sufficiently severe to justify modification of treatment. A possible explanation is given for this high incidence and for the remarkable occurrence of this side-effect in 39% of the control group.

The selection of cases suitable for long-continued chemotherapy is discussed.

One group of 28 cases received 15 mg. of prednisolone daily with the tetracycline, and in another group, of 27 cases, aminophylline 0·3 g. daily was added. The results in these two groups were remarkably similar in all respects and suggest that corticosteroids have little if any value as maintenance therapy in chronic bronchitis.

We are indebted to Dr. W. Williams and Dr. A. M. Brunton, of Messrs. Pfizer, for their assistance and for a supply of 'Tetracyn,' 'Delta-Cortril,' and the appropriate dummy tablets. Our thanks are also due to Dr. K. W. Cross for statistical advice; to Dr. R. J. Henderson for the bacteriology; and to Mr. R. W. Dillon for meteorological reports.

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"... what the true seeker after knowledge in his heart desires is some simple design which he feels must underlie the facts.... The search for principles which are æsthetically satisfying seems often frustrated by the complexity of nature, and the conflict between imagination and austere regard for truth seems often to result in the passage of scientific theories through three stages. The first is that of gross over-simplification, reflecting partly the need for practical working rules, and even more a too enthusiastic aspiration after elegance of form. In the second stage the symmetry of the hypothetical systems is distorted and the neatness marred as recalcitrant facts increasingly rebel against conformity. In the third stage, if and when this is attained, a new order emerges, more intricately contrived, less obvious, and with its parts more subtly interwoven, since it is of nature's and not of man's conception."—Sir CYRIL HINSHELWOOD, P.R.S., in his anniversary address to the Royal Society on Nov. 30.

ABSORPTION STUDIES ON RADIOACTIVE IRON-DEXTRAN IN PREGNANCY

LYNN A. J. EVANS *
B.Sc., M.D. Wales, F.R.C.S., M.R.C.O.G.
LATE REGISTRAR

N. W. RAMSEY
B.Sc. Lond., A.Inst.P.
PRINCIPAL PHYSICIST

CHARING CROSS HOSPITAL, LONDON, W.C.2

RADIOACTIVE iron has been much used in the study of iron metabolism, and its value in research is established. Iron-dextran complex (' Imferon ') has been successful in the treatment of iron-deficiency anæmia, and we have used this preparation, with isotopic iron incorporated, as a preliminary step in the elucidation of its fate in man.

We have studied the metabolism of iron-dextran in pregnant women, making use of ^{59}Fe-dextran complex. The rate of absorption from the site of injection in the gluteal-muscle mass has been studied for long periods. Some women were given ^{59}Fe-dextran complex in early pregnancy; these had been admitted for termination of pregnancy, with the exception of one patient with severe iron-deficiency anæmia in association with a normal pregnancy. In all these cases the pregnancy was of less than twenty weeks' duration. Others were investigated in late pregnancy; they were known to have a gross fœtal abnormality. One was given ^{59}Fe-dextran in the puerperium. Transfer of the isotope to the fœtus will be discussed elsewhere.

Material

Of the radioactive isotopes of iron, ^{59}Fe (half-life 45 days) is particularly suitable for routine work in which measurements of absorbed iron are made external to the body surface. But ^{59}Fe cannot be incorporated into iron-dextran complex simply by adding the isotope in ionic form. The complex is so stable that little or no exchange of iron can be expected. It was therefore necessary to produce, on a laboratory scale, material as similar as possible to the standard commercial product, but using ^{59}Fe Cl_3 as part of the starting iron solution. In this way an iron-dextran complex was produced with ^{59}Fe activity corresponding to 4 microcuries (μc). per ml. and a total iron content of 50 mg. per ml.

The labelled complex will be referred to as ^{59}Fe-dextran. It complied with all the tests applied to the commercial product ' Imferon.' Nevertheless, having regard to the circumstances of its preparation, the ^{59}Fe-dextran may not be identical in all respects with the standard manufactured iron-dextran complex. In the test for intramuscular absorption in rabbits (Beresford et al. 1957) the ^{59}Fe-dextran used in the present studies gave figures of 93·3 and 92·6% absorbed in 7 days.

The radioactivity of the tracer doses used in this research was too small to have any significant effect on the tissues. The calculated dose-rate to either ovary, in any of the women in whom studies were made, did not exceed the maximum permissible dose-rate for continuous exposure, which is given in the recommendations of the International Commission on Radiological Protection as 0·3r per week. During the studies, ^{59}Fe was observed to concentrate in the liver and spleen. The estimated maximum dose-rate in these organs was in no case greater than 0·3 rem per week during the peak uptake period.

Methods

Surface Counting

The ^{59}Fe-dextran was administered intramuscularly into the buttock by the technique usual in clinical practice. In some patients only one buttock was used; in others injections were made on each side, and the rates of absorption at the two sites compared. The material (2–3 ml.) was deposited either as a single pool or in three adjacent pools, with a view to comparing absorption-rates.

The apparatus used for surface counting was a wide-angle directional scintillation-counter, incorporating a thallium-activated sodium-iodide crystal, $1^1/_2$ in. in diameter and 1 in. thick. The field of view was approximately a 20 cm. diameter circle at a distance of 5 cm. from the front of the collimator; this diameter sub-tends an angle at the crystal centre of about 100°. A rate-meter was used to give a direct indication of count-rate.

The scintillation-counter was applied to the skin at a point directly over the injection-site, and always at the same angle to the body-surface. Observations were also made on some patients with the counter directed towards the liver and the spleen, in the same manner. Surface-counts were also made over the vastus lateralis at a distance below the site of injection corresponding to the distance of the midpoint of the liver or spleen above the injection-site. This was done to allow for the contribution to the count of activity in the blood. Readings were taken within a few minutes of the injection, at a few hours later, and at daily intervals for about a week. Thereafter measurements were made at increasingly longer intervals up to 4 months. By this time, the activity present was barely distinguishable from background radioactivity. Corrections for variations in counter sensitivity were determined at each clinical measurement by measuring the activity of a standard source of radioactivity under standard geometrical conditions. Corrections were also applied for radioactive decay.

The results of measurements over the injection-site were plotted as a percentage of the initial reading, taken a few minutes after injection. It was suspected, during the measurements in the earlier patients investigated, that the presence of ^{59}Fe in the liver or spleen was affecting the readings over the injection-site, and subsequently correction was made for this effect. Similarly the readings over the liver and spleen were corrected for the activity still present at the injection-site. It has not been possible to make a correction for errors arising from the known accumulation of iron-dextran in regional lymph-glands (see below). Owing to the difficulties of determining, by external counting, the radioactive content of internal organs (Corbett et al. 1956), surface-counts were plotted for the liver and spleen measurements; these cannot be computed as a percentage of the injection-site readings.

In an attempt to obtain data on the movement of the ^{59}Fe from the injection-site, readings were taken at successive increments of distance from the site of injection. After background due to general body radioactivity had been allowed for by shielding the injected region, graphs were drawn relating the reciprocal of the square-root of the reading to the distance of the counter from the skin. By extrapolation, the apparent depth of the material below the skin was obtained.

Further evidence was sought of the localisation of the ^{59}Fe by scanning the region of the injection-site and the external iliac fossa with a scintillation detector fitted with a narrow-angle collimator. The angle of view was 12° and the area of skin in the field of observation was a circle of 4 cm. diameter. The detector moved along a motorised horizontal traverse, with the patient lying horizontally on a couch below. The rate-meter readings were recorded automatically on a moving chart.

Blood content of ^{59}Fe

In one case serial blood samples were taken up to 7 days after injection, and the activity determined in plasma and whole blood. Red-cell ^{59}Fe content was calculated using the hæmatocrit reading.

* Now Senior Registrar, St. Thomas's Hospital, London, S.E.1.

Clinical Survey

Case 1.—A primigravida, aged 42, weight 106 lb., was admitted 10 days after her expected date of delivery in spontaneous labour. The first stage lasted 17 hours 30 minutes. After 50 minutes in the second stage the fœtal heart-rate had risen to 160 a minute and the liquor was meconium-stained. Examination revealed transverse arrest of the fœtal head. The fœtal head was rotated and the baby extracted using Kielland forceps under local bilateral pudendal-block anæsthesia. Delivery of the placenta was followed by a postpartum loss of 30 oz. of blood, part of which was derived from the episiotomy. A male infant was delivered, weighing 7 lb. 11 oz., with no evidence of asphyxia.

On the 2nd day of the puerperium hæmoglobin content was 52%, packed-cell volume (P.C.V.) 23%, and mean corpuscular hæmoglobin concentration (M.C.H.C.) 33%. On the 3rd day an injection of ^{59}Fe-dextran was given into each buttock. In the upper outer quadrant of the right buttock 2 ml. (4 μc.) was given as a single pool, and in the left buttock 2 ml. was given as three pools. Her anæmia was treated with 1500 mg. of iron as iron-dextran complex, 250 mg. being given daily into each buttock.

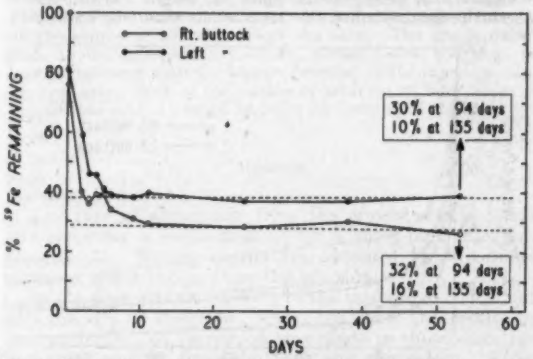

Fig. 1—Case 1. Absorption-curve derived from surface counts over the injection-sites (uncorrected).

The pattern of this patient's absorption of intramuscular iron isotope was not significantly different when the single pool was compared with the three-pool injection (fig. 1).

The activity recorded on the right side increased slightly 4 days after injection, coinciding with either the fixation of iron in the regional lymph-nodes or the uptake of isotope by the liver. The role of lymph-node absorption is discussed later.

The early rapid fall was of the order of 40% in the first day for the single pool and 30% for the three pools. The "slow" absorption was at the rate of 0·1% per day for the single pool and 0·25% for the injection given as three intra-muscular pools.

Case 2.—A primigravida, aged 20, weight 112 lb., was admitted for termination of pregnancy at 11 weeks. Her hæmoglobin was 94%. On the day of admission an injection of ^{59}Fe-dextran was given into the gluteal mass in the upper and outer quadrant. In the right buttock 4 ml. was given as a single pool, and in the left buttock 4 ml. as a three-pool injection. Because of decay of the isotope, the dose was about 4 μc. in each depot.

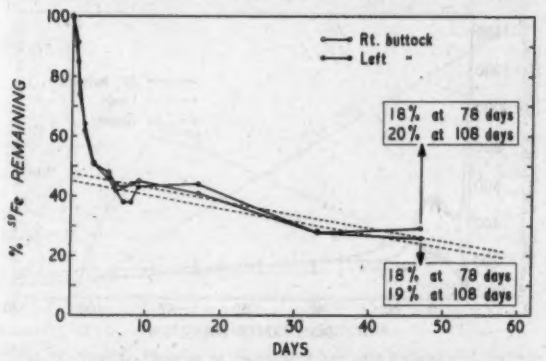

Fig. 2—Case 2. Absorption-curve (uncorrected).

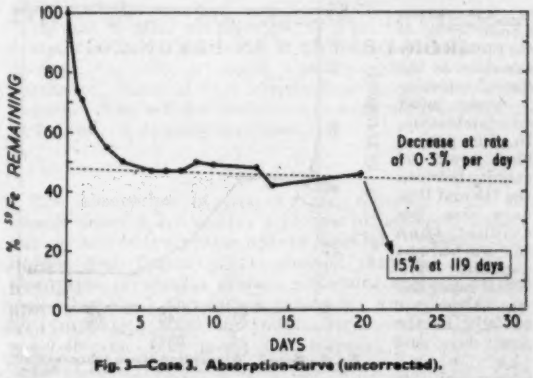

Fig. 3—Case 3. Absorption-curve (uncorrected).

Pregnancy was terminated 48 hours after the injection of ^{59}Fe-dextran. After discharge from hospital the patient attended for subsequent estimation of the residual ^{59}Fe at the site of the injection. The initial rate of iron absorption was rapid (fig. 2), over 50% being absorbed by the end of the first week. There was no significant difference between the rates of absorption from the two sides. Fig. 2 illustrates an increase in activity recorded between the 8th and 10th days after the injection. The rate of "slow" absorption was about 0·25% of the dose per day, compared with about 20% during the 1st day after injection. By the 108th day, the surface count had fallen to 20% of its initial value, for both sides.

Case 3.—A woman, aged 31, weight 133 lb., was admitted with a diagnosis of polyarthritis in early pregnancy. 6 days before admission she noticed the onset of tingling in her hands and feet and severe interscapular pain; on the day before admission she had pain in her ankles, knees, shoulders, elbows, and hands. Her general condition was satisfactory and her temperature normal. Movement of her cervical spine was limited. Synovial effusions were present in her right ankle, both knees, and metacarpophalangeal joints. Movement of her left hip and left elbow was grossly limited by pain. Many investigations gave virtually normal findings. ^{59}Fe-dextran was given into the left gluteal muscle mass in a dose of 3 ml. (equivalent to 6 μc.). At this time her hæmoglobin was 105%, red blood-cells 5,100,000 per c.mm., P.C.V. 45%, mean corpuscular volume 88 c.μ, M.C.H.C. 34%. 45 hours later the pregnancy was terminated by an abdominal hysterotomy, when the uterus corresponded in size to an 18-week cyesis.

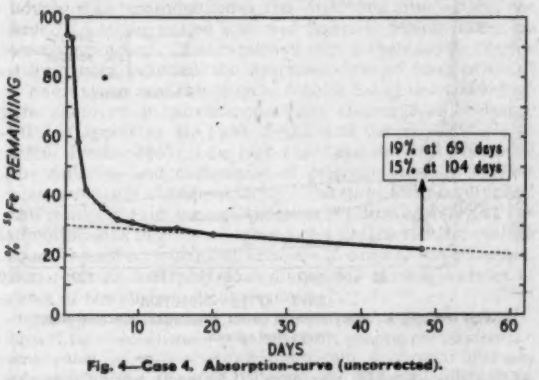

Fig. 4—Case 4. Absorption-curve (uncorrected).

The patient was in hospital for 3 months and for most of this time was confined to bed being treated with cortisone and analgesic drugs and by the physiotherapy and orthopædic units for her joint lesions. Apart from sitting in a chair for short periods, she was relatively immobilised in bed for 5 weeks following the injection of ^{59}Fe-dextran. Her iron absorption (fig. 3) left a greater residue than any other patient's

in this series. About 50% of the radioactivity remained at the site of injection 2 weeks after administration. In this patient the peak of activity between the 7th and 10th days was less evident than in ambulant patients. The initial rapid fall was at the rate of 30% in the first day, and the "slow" absorption at the rate of 0·3% per day.

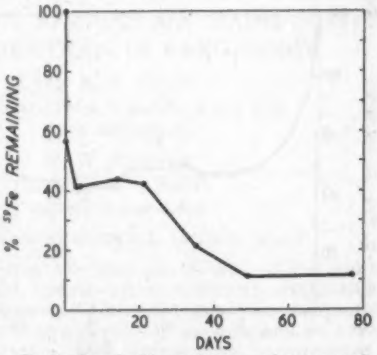

Fig. 5—Case 5. Absorption-curve (uncorrected).

Case 4.—A primigravida, aged 25, weight 126 lb., whose general condition was satisfactory, was admitted for treatment of anæmia. The uterus corresponded in size to a 12-week pregnancy. Her hæmoglobin was 53%, red blood-cells 3,280,000 per c.mm., colour index 0·69, P.C.V. 29%, M.C.H.C. 30%. A film showed obvious anisocytosis, poikilocytosis, and hypochromia.

On the day of admission a dose of ^{59}Fe-dextran equivalent to 6 μc. in a volume of 3 ml., was injected as a single pool into the upper outer quadrant of the right buttock. There was a rapid uptake of radioactivity but no peak between the 7th and 10th days (fig. 4). The patient was subsequently treated with daily injections of iron 250 mg. as iron-dextran complex in the left buttock, to a total dose of 1500 mg.

The absorption curve derived from the surface count-rate was remarkably smooth. The fall in activity the 1st day was 7% and in the 2nd day 37%; the "slow" absorption was

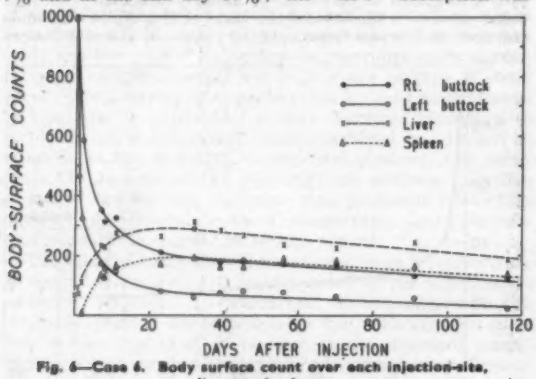

Fig. 6—Case 4. Body surface count over each injection-site, liver, and spleen.

at the rate of 0·14% per day. It is worth noting that this patient was iron-deficient at the time of injection, as was case 6. In both cases a therapeutic course of iron-dextran complex was not given until the early absorption of the isotope had been measured.

The amount of radioactivity excreted in the urine from the 2nd to the 6th day and in fæces from the 2nd to the 5th day was assayed. No activity was found, the standard deviation of the count-rate being equivalent to 0·14% of the dose.

Case 5.—A woman, aged 24, weight 146 lb., had a normal pregnancy until the 36th week, when an anencephalic fœtus was diagnosed and confirmed radiologically. At the 39th week of pregnancy an injection of ^{59}Fe-dextran 4 ml. (8 μc.) was given into the upper outer quadrant of the left buttock; labour was then induced.

The hæmoglobin content was 73% on the 2nd day after delivery (it had been 84% at 10 weeks), and 65% on the 7th day, with P.C.V. 35% and M.C.H.C. 29%.

The pattern of the absorption curve in this patient (fig. 5), though in outline similar to that in the other cases was unusual. 3 weeks after the injection of radioactive iron-dextran, the level of the "slow" absorption curve fell from 40% to about 10% over about 24 days, and then continued at rather less than 0·1% per day. The initial rapid fall amounted to about 50% in the 1st day. A small rise in activity was recorded at 14 days.

Case 6.—A woman, aged 32, weight 126 lb., was admitted for termination of pregnancy. The size of the uterus was consistent with the period of amenorrhœa (12 weeks). A single injection of ^{59}Fe-dextran 5 μc. was given into each buttock, and 2 days later pregnancy was terminated. On admission the hæmoglobin was 62%, P.C.V. 32%, M.C.H.C. 29%. Her anæmia was treated subsequently by imferon.

Surface counts recorded over the buttocks, liver, and spleen, showed little rise in activity over the injection sites during the 2nd week (fig. 6). The "slow" absorption rates were 0·8% per day for the right side, and 0·07% for the left (fig. 7).

Case 7.—A primigravida, aged 22, weight 155 lb., had a normal pregnancy until the 32nd week, when she had acute

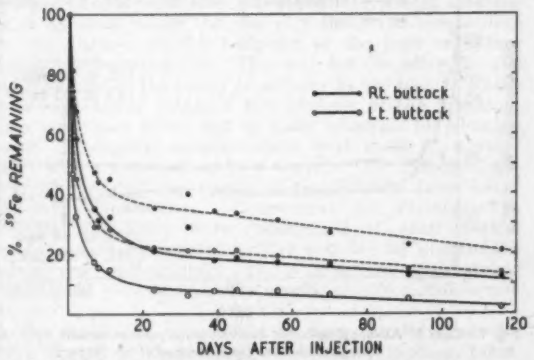

Fig. 7—Case 6. Absorption-curves derived before (uncorrected, broken line) and after (corrected, solid line) allowance for activity in liver and spleen.

hydramnios. Radiography showed an anencephalic fœtus. An injection of 4 ml. (about 8 μc.) of ^{59}Fe-dextran was given as a single pool in the right buttock at 33 weeks. At this stage of pregnancy the hæmoglobin was 71%, P.C.V. 31%, M.C.H.C. 34%. Labour was induced by artificial rupture of the membranes followed by an oxytocin drip.

The liver and spleen content of isotope fell distinctly between the 13th and 17th days after injection (fig. 8). Thereafter the fall was much slower, decreasing eventually to a rate of 0·1% a day. A rise in activity over the site of injection was recorded between the 8th and 13th days. This was thought to be due to an inadequate correction for liver activity. But the large "hump" in the graph (as in case 5) may be partially attributable to the presence of an actively involuting uterus. The altered lymph-drainage and blood-flow of the pelvis at this time may have contributed towards the hump in the activity regression curves of both patients.

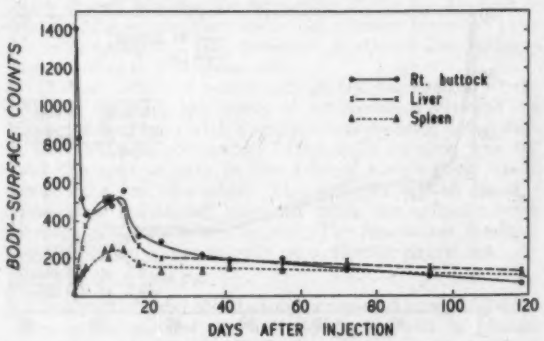

Fig. 8—Case 7. Body surface counts over injection-site, liver, and spleen.

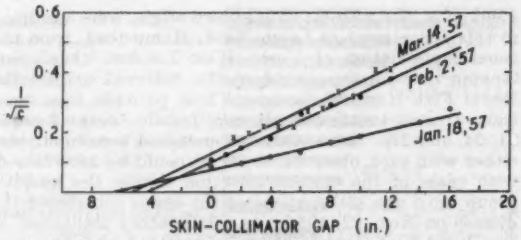

Fig. 9—Case 7. Injection of 8 μc. in right buttock on Jan. 1.

Reciprocals of the square-roots of the count-rates are plotted as ordinates, and the distances between the patient's skin and the collimator as abscissæ. The detector was pointed directly towards the anterior surface of the patient over the injection-site. From the intercept on the axis of abscissæ, a distance of 2 inches should be subtracted to give the depth of the source of activity below the skin. The graph dated Jan. 18 indicates activity at 4½ inches below the skin, in good agreement with the known position of the injection-site. The apparent shift of the source of activity at later dates is compatible with a partial anterior movement of the activity.

Results

External Counting

The rate of absorption from the gluteal site is much the same for a single-pool as for a three-pool injection (figs. 1, 2). Similar results are obtained for injections given in either the right or the left side.

In the first 3 days, 50–60% of the injected activity had left the site of injection. Figs. 1–5 show the results in five patients; no correction was made in these cases for radiation pick-up from the liver and the spleen. After the first 10 days the absorption-rate was much reduced, eventually falling to a rate of decrease of 0·1–0·33% a day. Fig. 7 illustrates the effect on the local-absorption curve of correcting for the presence of activity in the liver and spleen. Figs. 6 and 8 further demonstrate the patterns of absorption over the injection-site, liver, and spleen, when similarly corrected. There was a striking uptake in the liver and spleen, reaching a peak which varied between the 10th and 20th days after injection in different patients.

The inverse-square-law measurements (fig. 9) were not sufficiently precise, owing to low count-rates, to give more than an approximate localisation of activity. The evidence, though slight, confirms that much of the isotope moves from the injection-site to the regional lymph-nodes (Cappell et al. 1954, Evans 1957). In case 6, on the 56th day, when 20% of the dose appeared to remain in the buttock, scanning showed an appreciable activity in the iliac fossa over the regional lymph-nodes. Similar results were obtained in case 7.

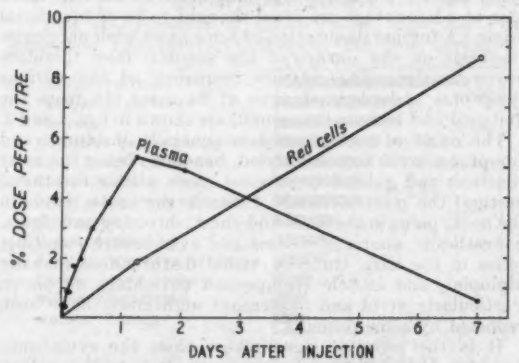

Fig. 10—Case 8. Transfer of radioactive iron into plasma and red cells from intramuscular injections.

Blood Activity

In case 8, after an injection of 5 μc. the plasma-^{59}Fe content reached a maximum in 30 hours with subsequent decrease (fig. 10)—a course which parallels closely the results of chemical iron estimations in patients given imferon. The red-cell activity has been recorded for up to 7 days; it steadily increased.

Discussion

The absorption of iron-dextran complex from the muscle depot is not merely a process of passive diffusion, but an active lymphatic uptake from the injection-site. Barnes and Trueta (1941) showed that the route of absorption of various protein molecules depends on the molecular size; the larger molecules are absorbed by the lymphatic system, and the smaller ones directly by the blood-stream. The mode of absorption of iron-dextran complex following intramuscular administration has been proved to take place by a lymphatic route (Beresford et al. 1957, Golberg 1957, Evans 1957). The rate of appearance of activity in the plasma in case 8 is in accord with lymphatic absorption of ^{59}Fe-dextran.

One implication of these findings is the need for active lymph-flow before absorption can take place. In this respect the immobilised patient is at a disadvantage, as in case 3, where retention of the isotope in the muscle mass after injection was appreciably higher than in any other case. This patient was partly immobilised on account of polyarthritis, and the restriction in muscle lymph-flow presumably played a major role in the delay in absorption. The fact that she was on cortisone treatment at this period may also have affected the process of "reactive absorption" (see below).

The results of the absorption-rates of ^{59}Fe-dextran from the site of injection in the gluteal muscle mass suggested at first that there might be two components present in iron-dextran: a rapidly absorbed fraction, which was removed from the injection site within the first 7 to 10 days, and a second fraction, which was more slowly absorbed. The results of this investigation show a discrepancy between the apparent rate of absorption of ^{59}Fe-dextran and the clinical results using imferon which are achieved in anæmic patients (Baird and Podmore 1954, Cappell et al. 1954, Scott and Govan 1954, Scott 1956, Evans 1957). In fact the data illustrate some of the fallacies and difficulties of interpretation in surface measurements of radioactivity. Taken at their face value, the results would suggest that the residual activity at the injection-site in patients does not parallel the low values found by direct chemical analysis in animal experiments. But such an interpretation disregards several sources of error in the surface measurements:

The effect of accumulation of ^{59}Fe in the liver and spleen.—It will be recalled that, in some of the graphs portraying the absorption of radioactive iron-dextran, a distinct increase in activity was recorded between the 7th and 10th days. In view of the peak of activity recorded in the liver in the later patients at about this interval, it is probable that the apparent increase was due more to liver and spleen activity than to the amount of ^{59}Fe deposited in the regional nodes.

The concentration of iron-dextran in regional lymph-glands close to the injection-site (Cappell et al. 1954, Golberg 1957, Golberg et al. 1957, Evans 1957).—The lymphatic drainage of the skin and superficial fascia of the gluteal region is to the superficial inguinal lymph-nodes. The deep lymphatics of the gluteal muscles pass to the external iliac lymph-nodes. Stevens (1957), investigating the rate of absorption of ^{59}Fe-dextran, injected it into the substance of vastus lateralis above the knee-joint. He recorded similar increases of activity in the femoral and iliac group of lymph-nodes and found the total absorption to be 90% in 5 days in both normal and iron-deficient patients.

In a detailed study of the mechanism of the absorption of iron-dextran complex, Golberg (1957) has divided the process into stage I (consisting of rapid "reactive absorption," and lasting about 48–72 hours) and stage II (the

process of " macrophage transfer," which is very gradual and continues over a long period). These stages are reflected in our observations. Some of the iron becomes fixed in connective tissue surrounding the muscle-fibres and is not removed from the injection-site, thus accounting for some of the residual activity present in this region. But in view of Stevens' observations, a large proportion of the residual activity observed may be due to the ^{59}Fe still present in regional lymph-glands. It is clear, therefore, that when all the factors have been taken into account the proportion of unabsorbed material is very low in most cases.

Conclusions

About 80% of a dose of ^{59}Fe-dextran, given intramuscularly in the gluteal muscle mass, is absorbed within 3 weeks of injection. Recorded activity continues to diminish, at a reduced rate, for a period which may be as long as 6 months. The rate of appearance of the radioactivity in the blood confirms a lymphatic route of absorption from the intramuscular site.

Activity over the liver and spleen reaches a maximum in 10 to 20 days. In interpreting surface-activity measurements, account must be taken of the contribution made by iron accumulation in liver, spleen, and regional lymph-glands draining the injection-site.

^{59}Fe-dextran complex was provided by Benger Laboratories Ltd. The work was done with the permission and approval of the advisory panel of the Medical Research Council.

Our thanks are due to the consultants at Charing Cross Hospital for permission to investigate patients admitted under their care, and to the director of research at Benger Laboratories, Ltd., for the supply of the isotope and help in the preparation of this paper. One of us (L. A. J. E.) is indebted to the editors of the University of California Press for permission to publish this work, which was included in a lecture given at the International Symposium on Iron Metabolism at the University of California, which is being published in book form; and to the Clinical Research Committee of Charing Cross Hospital for a personal research grant.

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ENCEPHALOMYELITIS IN NORTH WEST LONDON

AN ENDEMIC INFECTION SIMULATING POLIOMYELITIS AND HYSTERIA

A. MELVIN RAMSAY
M.A., M.D. Aberd.
PHYSICIAN, INFECTIOUS DISEASES DEPARTMENT, ROYAL FREE HOSPITAL, LONDON

SPORADIC cases of encephalomyelitis simulating poliomyelitis in North West London in 1955 (Ramsay and O'Sullivan 1956) formed the background to the sudden explosive outbreak of an unknown infection of the central nervous system among the staff of the Royal Free Hospital Group (Compston 1956, Richardson 1956, Dimsdale 1957, Crowley et al. 1957, *British Medical Journal* 1957). Although there has been no further institutional outbreak, the infection is still prevalent.

Between April 20, 1955, and Jan. 7, 1956, 16 cases of this type of infection, variously diagnosed as poliomyelitis, meningitis, and pyrexia of unknown origin, were admitted to this department at Lawn Road, Hampstead, from the general population of North West London, thus overlapping in time the period of the outbreak within the Royal Free Hospital Group. These patients were aged from 9 years to 45, and all were female except 3 (aged 21, 24, and 27). None of the patients had been in contact either with each other or, so far as could be ascertained, with cases of the current infection within the hospital group until the 13th patient of the series contracted the disease on Nov. 22, 1955. As a laboratory technician at the Royal Free Hospital, Gray's Inn Road, she may have been in contact with a carrier of the infection; and the next patient, a laboratory technician at another hospital, had paid social visits to the laboratory at Gray's Inn Road.

After January, 1956, there was an interval of nearly five months during which no case of the disease was seen in this department; but on June 1, 1956, a nurse from the Royal Free Hospital's preliminary training school (situated about a mile to the west of the hospital at Lawn Road) was admitted with fifteen days' history of earache, frontal headache, retro-orbital pain, giddiness, nausea, and vomiting (Geffen 1957, Geffen and Tracy 1957). She had weakness of her right arm and right leg, and ultimately a classical serratus palsy with " winged scapula ". Because of the extent of the paresis she was at first thought to have poliomyelitis; but much-exaggerated tendon-reflexes, the late development of acute muscle tenderness in all the muscles of the right side of her body, and electromyography rendered this diagnosis untenable.

6 further cases from the preliminary training school, exhibiting a similar pattern of infection, occurred within the next two weeks and were isolated in this department; electromyography was not done in these cases, because of the risk of spreading the infection to other departments of the hospital. One nurse, who had been in contact with the first nurse from the preliminary training school for one day, one doctor, and a ward maid developed the disease, but fortunately the outbreak within the hospital went no further. Between June 17 and Aug. 8, 1956, however, 8 sporadic cases of the infection were admitted from various parts of North West London and, as in the previous year, these cases had no apparent connection with each other or with the cases within the hospital. The 1956 patients were aged 18–44, and all were female except a doctor, aged 32. After August, 1956, there was again an interval of five months with no cases, but since January, 1957, 12 cases have already been treated and others are under observation.

Clinical Picture

The clinical picture has been described by several workers, but it seems likely that, in the early stages, many cases are diagnosed as poliomyelitis whereas those seen at a later stage are often thought to be of functional origin. A further description of some cases with particular emphasis on the nature of the sequelæ may therefore prove timely. The relative frequency of the various symptoms and physical signs of 34 cases (16 from the first year and 18 from the second) are shown in figs. 1 and 2.

The onset of the infection is generally insidious, and symptoms are many and varied, headache being the most constant and giddiness (in most cases a true rotational vertigo) the most striking. Pains in the limbs, pains in the neck, pains in the back and chest, shivering and rigors, paræsthesiæ, anorexia, nausea and even severe vomiting, pains in the ears, tinnitus, visual disturbances (usually diplopia), and muscle cramps and twitchings all occur. Particularly vivid and unpleasant nightmares have been reported by some patients.

It is the physical signs rather than the symptoms, however, that distinguish this disease from poliomyelitis. In no instance was complete flaccid paralysis present, and

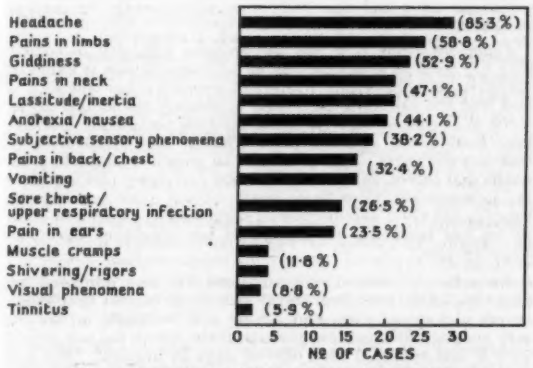

Fig. 1—Symptoms in 34 cases of encephalomyelitis.

contraction of the weak muscles against both gravity and resistance was possible, if only for a few seconds; most of them would have been graded 3 or 4 in the M.R.C. system. More striking features were the absence of wasting; tendon-reflexes which, though sometimes initially depressed, remained normal or became much exaggerated throughout the illness; sensory impairment persisting for weeks and months; and, in some cases, acute widespread muscle tenderness, clonus, or tremor, which, I must emphasise, was not necessarily present at the onset. These findings compelled us to suspect some other disease than poliomyelitis. Some patients appeared to have an infection of the upper respiratory tract, but the enlarged lymph-nodes were not a distinctive feature, being just as often seen in poliomyelitis and other virus infections of the respiratory tract. Pyrexia was usually low grade; only in 3 cases did it exceed 100°F at any time; most patients tended to have bouts of low-grade pyrexia throughout the illness, but some were completely apyrexial while under observation.

Blood-counts.—Nothing further can be added to our original observation (Ramsay and O'Sullivan 1956) that the blood picture was characteristic of a virus infection: a neutropenia with inconstant abnormal lymphoctyes.

Erythrocyte-sedimentation Rates.—The E.S.R. was estimated in 22 cases. It ranged from 2 to 13 mm. in the first hour (Westergren) with the exception of 2 cases; in one of these it was 50 mm. (although it was 3 mm. four days later), in the other 22 mm.

Cerebrospinal Fluid.—Lumbar puncture was done in 17 of the 34 cases. Excluding one blood-contaminated specimen, the C.S.F. was normal in every case except 2, 1 of which showed 8 cells (lymphocytes) and the other 50 mg. of protein per 100 ml. of fluid. Wassermann and Kahn reactions were all negative.

Special Investigations

Virus investigations in collaboration with the Virus Reference Laboratory, Colindale, did not reveal the

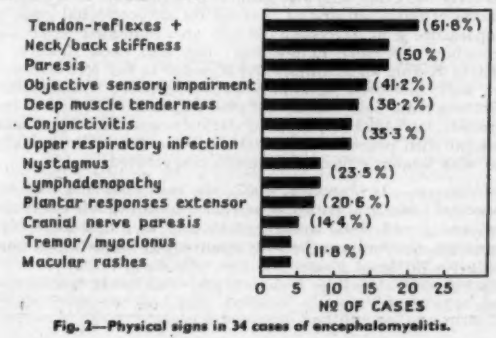

Fig. 2—Physical signs in 34 cases of encephalomyelitis.

ætiological agent. Throat washings and/or fæces were examined in tissue culture of monkey kidney for poliomyelitis and Coxsackie and other viruses. Screening by serological testing for lymphocytic choriomeningitis, mumps, leptospirosis, and all three types of poliomyelitis was negative in each case.

Electromyography.—All 16 patients in the first group and 10 of the second group were submitted to electrodiagnostic examination. All in the first group and 5 of the second gave the characteristic myogram (Ramsay and O'Sullivan 1956, Richardson 1956). The value of this abnormal myogram (fig. 3) lies in the fact that it shows no evidence of neuronal degeneration; since it is inconceivable that a large series of poliomyelitis cases, some with prolonged paresis, should not show neuronal degeneration, this fact eliminates poliomyelitis, even an aberrant form, from the diagnosis. The myogram undoubtedly indicates a pathological lesion, whose precise site, however, remains a matter of speculation; and in the absence of necropsy material it is hardly likely that we shall further our knowledge on this point.

Electro-encephalography was done in 6 patients (Ramsay and O'Sullivan 1956). The changes found were not specific but are interesting because similar recordings were obtained in encephalitis reported from Denmark (Pedersen 1956).

Sequelæ

The sequelæ of this disease provide further features which emphasise its wide divergence from poliomyelitis. It has been possible to follow up 26 of the 34 cases and the following are representative case-reports.

Case 1.—A married female domestic worker, aged 44, was admitted on April 20, 1955, with two days' history of headache, lassitude, and shivering.

On admission she was mildly confused and appeared to be uncooperative, probably because she could not maintain her

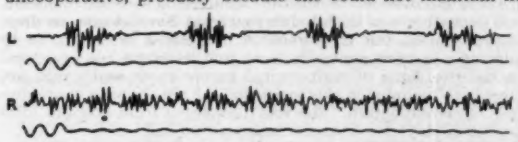

Fig. 3—Electromyograms: *upper register*, from left tibialis anterior muscle on maximal volition, showing grouping of large polyphasic motor-unit potentials; *lower register*, from right tibialis anterior muscle on maximal volution, showing complete interference pattern of normal motor-unit potentials. (Calibration 500 and 100 μV at 50 cycles per sec.)

attention when questioned. She kept grimacing, making masticatory movements, and licking her lips. Continuous clonic twitchings of the left side of her face and her left sternomastoid muscle, slight right ptosis, and bilateral weakness of her palate were present. Irregular pyrexia not exceeding 99·4°F persisted throughout her stay of thirteen weeks in hospital. The facial manifestations gradually subsided, but cramp-like distressing myoclonus affecting the whole of her left leg persisted. Her plantar responses became extensor (the right two days after admission, the left three days later) and returned to normal only after two months. Sensory disturbances were not observed, but her calf and quadriceps muscles were tender.

Follow-up examinations have shown gradual intensification of myoclonus in her left leg and a tendency to painful cramp, which compels her to remain motionless, though in obvious distress, until it subsides. The patient is fortunately of an extrovert type, accepting her disability and, so far as possible, ignoring it. She has been given full courses of both pyridostigmine ('Mestinon') and benzhexol hydrochloride without benefit and is now losing weight.

Case 2.—An unmarried female typist, age 26, with five weeks' history of bilateral loin pain, had her kidneys investigated with negative results at another hospital and was discharged with a diagnosis of hysteria. Three days later, on July 26, 1955, she was admitted to this unit with severe headache, stiffness of her neck, backache, occasional pains in her corvical and dorsal regions, and weakness of her left hand

and wrist. She also complained of a sense of pressure over her head, blurred vision, severe vertigo, a feeling of heaviness in her legs, shoulders, and upper arms, and what she described as a tremulous weakness most pronounced on the left side.

Follow-up examinations during the past two years have shown persistence of weakness and gross sensory impairment in her left leg below the knee. She is easily fatigued, tends to fall, and copes with her occupation as a shorthand typist with some difficulty. For some months she found herself unsure of her balance and therefore afraid in traffic.

Case 3.—A male instrument maker, aged 27, developed after five days' coryza and sore throat, numbness of the right side of his face, loss of taste over the right side of his tongue, and repeated attacks of vomiting and giddiness. During the next ten days he could not retain fluids and was admitted to the unit on Aug. 27, 1955.

On admission the patient had bilateral nystagmus; no sensation to fine touch over the distribution of the right fifth cranial nerve; hyperæsthesia to pinprick over the same area; normal temperature sensation; mild paresis of the right side of his face, with deviation of his tongue on protrusion to the right; and no taste sensation over the whole of the right side of his tongue.

Follow-up.—He has been seen on two occasions since discharge from hospital; he feels well and has returned to his occupation of precision engineering. He found it difficult to concentrate at first and experienced a sense of unbalance if the room was plunged into darkness or when he stood upright after washing at the basin. He experiences frequent muscle cramps in his right foot and calf muscles and has a burning sensation along the edge of his tongue as far as the corner of his mouth, and the right side of his face feels stiff and mask-like and does not relax as well as the left. All his tendon-reflexes are easily elicited, and his knee- and ankle-jerks are abnormally brisk; his plantar responses are now flexor. Eighteen months after the onset he still had complete loss of taste perception over the whole of the right side of his tongue.

Case 4.—A married woman, aged 45, was admitted on Nov. 9, 1955, with five weeks' history of shivering attacks, lassitude, and paræsthesiæ in both hands and feet. She did not complain of sore throat, but on admission her fauces were seen to be infected. She felt generally weak and lethargic but presented no definite signs of neurological involvement and could not have been included in this series had she not shown a characteristic electromyogram. She was discharged from hospital after seventeen days for domestic reasons but still not fit.

Follow-up examinations show that a tendency to physical and mental fatigue still persists but is becoming less severe. After an attack of mild sore throat in October, 1956, she had a severe recurrence of symptoms, with complete exhaustion and much-exaggerated tendon-reflexes in both arms and legs—a feature that had not been noted in the original attack.

Case 5.—A male student, aged 21, was admitted on Jan. 7, 1956, with five days' history of lethargy, inertia, pains in his neck and limbs, and headache. He was apyrexial throughout his stay in hospital. He had pain on full flexion of his neck, and enlarged cervical glands. All his tendon-reflexes were exaggerated, and muscle tenderness was present in both trapezius muscles. Four days after admission he had paræsthesiæ in his arms and legs for four or five days. No objective signs of sensory impairment were detected. He was discharged from hospital apparently fit after twenty-one days.

Follow-up.—Six months later he reported that, shortly after leaving hospital, he had experienced a recurrence of severe frontal headaches, pains in the limbs, and general weakness. A tendency to fatigue persisted, and he was compelled to discontinue his studies as well as other jobs which he had undertaken.

Case 6.—A married woman, aged 26, was admitted on June 17, 1956, as a case of pyrexia of unknown origin and meningitis, with seven days' history of frontal headache, retro-orbital pain, severe photophobia, anorexia, and vomiting unassociated with food. Except for two peaks of temperature to 99°F she was apyrexial throughout her stay in hospital. She had particularly severe photophobia for six days after admission, slight neck stiffness, and a positive Kernig sign. Her tendon-reflexes were increased in her left arm and leg, but power and sensation were normal. She had slight right-sided facial weakness. Her C.S.F. contained 8 cells per c.mm. but was otherwise normal. She was discharged from hospital after seventeen days and has been seen subsequently on several occasions.

Follow-up.—She now has the greatest difficulty in coping with her work as a cleaner and as a housewife and is liable to outbursts of temper and hysterical weeping; her memory is bad, and she cannot trust herself to manage the simple arithmetic of housekeeping. At times she feels completely lost and may find herself in some place without any recollection of how she got there. She is subject to painful cramps in both hands and calves, drops articles easily and, after picking them up, immediately drops them again. Until quite recently she experienced vivid and distressing nightmares; these now seem to be less insistent, but otherwise her condition shows no improvement.

Case 7.—A married woman, aged 41, was admitted on June 10, 1956, with four days' history of frontal headaches, severe abdominal pain, and aching and weakness in her left arm and leg. She had low-grade pyrexia, which did not exceed 99·6°F and subsided after eleven days in hospital. She had some neck stiffness and a positive Kernig sign, mild conjunctivitis, persistent and troublesome photophobia, considerable weakness of her left arm and leg, and widespread deep muscle tenderness over the whole of her left side. Three days after admission she complained of pain in her right arm and vomited profusely; five days later she had left-sided facial anæsthesia, which subsequently spread to her left arm and leg. The muscles of the left side of her neck, upper arm, and (to a less extent) her left leg became extremely tender and the tendon-reflexes much exaggerated. She was discharged from hospital after fifty-seven days, with extensive neurological involvement.

Follow-up.—In May, 1957, she showed no improvement, having lost all sensation in her left leg which did not feel as if it belonged to her and was held in a state of poker-like rigidity. Sensory perception was greatly diminished in her left arm but not so much as in her leg. She had become extremely irritable, and small incidents upset her. Her menstruation was irregular, and she was rapidly putting on weight. There was a reversal of sleep rhythm, with the result that she required amphetamine by day and barbiturates at night.

Case 8.—A married woman, aged 44, was admitted on July 21, 1956, with three days' history of headache, vomiting, and weakness and paræsthesiæ in her left arm and leg. She was practically apyrexial throughout her stay in hospital. She had weakness and glove-and-stocking anæsthesia in her left arm and leg and much-exaggerated tendon-reflexes. Her plantar responses were flexor. Her C.S.F. was normal. She made very little progress during her twenty-seven days in hospital. She was highly emotional and subject to bouts of uncontrollable weeping.

Follow-up.—Her subsequent course was characterised by severe relapses, of which two were more severe than the original attack. Her private doctor states that she has always been neurotic, and much of her condition may have been functional. Nevertheless electromyography showed the features characteristic of the disease.

Case 9.—A married woman, aged 37, developed headache and backache while on holiday in Devon on July 26, 1956. On Aug. 5 she vomited, and next day she had stiffness of her neck, her backache was worse and she had dizziness on sitting up and numbness and coldness of her left hand and leg. She resumed her household duties on Aug. 7 but had sore throat and fever next day and was admitted to the unit as a case of pyrexia of unknown origin. Except for an occasional peak of temperature not exceeding 99·2°F she remained apyrexial throughout her stay in hospital She had neck rigidity, a positive Kernig sign, diminished a power in her left arm and leg, and increased tendon-reflexes; sensory impairment, involving pain, light touch, and position, in her left arm; and normal C.S.F. After twenty-four days she was discharged from hospital with practically normal sensation but walking badly and with tendon-reflexes still much exaggerated.

Follow-up.—In January, 1957, she said that she had not improved; she still had pins-and-needles in her left hand and foot and found that, though previously of an equable temperament, she had now become emotionally unstable and was liable to bursts of temper on the mildest provocation. She dropped objects readily, had vivid and frightening nightmares, and became very readily fatigued. She had lost power in her left arm and leg and had impaired sensation of the glove-and-

stocking type. In March, 1957, she had completely lost joint sense in her fingers and toes on the left side, had pronounced muscle tenderness in her left calf, and tended to sweat severely by day and by night. The Romberg sign was mildly positive. In April, 1957, her condition was worse: her left hand and foot were mauve and felt colder than her right arm and leg. She had a pronounced intention tremor. In June, 1957, her left leg jerked involuntarily in clonic fashion, and this would take up to five minutes to pass off. She was very unsteady in walking and had hypo-algesia of the whole left side of her body, with complete loss of position sense in her left foot. Although her nightmares had ceased, she had uncontrollable attacks of temper accompanied by feelings of unreality and olfactory hallucinations of blood; excessive frigidity had made sexual intercourse impossible; and the strain on her domestic relationships was having a noticeably adverse effect on her youngest child.

Case 10.—A married woman, aged 36, was admitted on July 31, 1956, with five days' history of pain in ner neck, headache, attacks of transient giddiness, shivering, and frequent vomiting. She had low-grade pyrexia not exceeding, but frequently, 99° and 100°F for the first ten days in hospital; this finally settled to normal after the sixteenth day in hospital. She had much neck rigidity and could not kiss her knees. She complained of tiredness in both arms, which felt as though she had been lifting a heavy weight. There was weakness of all muscle groups in her left arm and slight weakness of flexion of her left hip. Her tendon-reflexes were much exaggerated but her C.S.F. was normal. She was still walking badly when discharged from hospital after thirty-one days.

Follow-up.—She reported that, although fresh in the morning, she tired very readily in the afternoon and was prone to emotional upsets. There was still weakness of all the muscle groups in her left leg.

Discussion

The patients with neurological involvement usually recovered slowly. In those with pareses there is still no evidence of wasting even after two years, and some of those who had sensory loss still show impairment, in 1 case total. Severe neuralgic pains in head or limbs, epigastric pain and nausea, paræsthesiæ of various kinds affecting both the limbs and trunk, tinnitus, visual disturbances, and nightmares have all proved troublesome sequelæ. Even more striking has been the persistence or development of a peculiar volitional tremor with slight incoordination and a jerky cog-wheel-like muscle action which reflects perfectly the condition shown by the myogram—i.e., a burst of activity followed by quiescence. As might be expected, these patients show a mildly positive Romberg sign—i.e., though not actually falling they have difficulty in retaining their balance with closed eyes. Many who are otherwise completely recovered report that they tend to drop, or even fail to grasp, articles, especially when tiring toward the end of the day, and the destruction-rate of their household crockery has in consequence risen alarmingly. Myoclonus or spasm present in some cases on admission has invariably persisted and in 2 cases is becoming more pronounced.

All the patients, whether with or without neurological involvement, have shown two characteristic and very insistent sequelæ:

(1) *Proneness to Fatigue.*—Even the youngest patients testify to the ease with which they become both physically and mentally fatigued, and this may persist for weeks or months after the attack. It was well exemplified in a schoolgirl, aged 15, who had been outstanding both at work and play; she was particularly extrovert and vivacious, and although she had weakness and a patch of blunting of sensation in her right leg, she was not obviously encephalitic during her three weeks' stay in hospital. Yet for six months after her return to school she was compelled to go to bed every afternoon at 5 P.M. and could not attempt her homework. After six months her condition gradually resolved, she is now fully restored, and her physical and mental powers appear to be unimpaired. Older patients, including students not included in this series, report that their physical and mental power is still below normal.

(2) *Emotional Lability.*—This is probably present in every case but manifests in inverse ratio to the inherent stability of the psyche. Most patients exhibit outbursts of irritability and hysteria, which have proved very distressing to those who, previously of a calm and equable temperament, are fully aware of a change in disposition which no conscious effort of the will can control. One patient who, before her attack, had been described as the life and soul of the party became introspective and subject to bouts of uncontrollable weeping, lacked confidence to meet people, and was terrified to go out alone in traffic (this was a common feature in other cases also). She was finally referred for psychiatric supervision; she received a course of modified insulin-shock therapy without apparent relief but is now at last showing some sign of returning to normal and for the first time has lately summoned up sufficient confidence to visit the hospital unaccompanied. It is still too early to expect improvement in case 9, who provides the most sinister example of disturbances of the psyche in our series. It is quite understandable that a neurologist seeing these patients with their bizarre jumble of neurological signs and emotional disturbance is likely to diagnose hysteria. Indeed the hysterical nature of certain features in the clinical manifestation is obvious. Nevertheless it constitutes a grave injustice to diagnose hysteria in these cases without recognising that the condition is organically determined.

Although periodic remissions are likely, the general tendency is toward slow improvement; but in cases with gross neurological involvement permanent disability appears to be likely, and this is borne out by the follow-up examinations made by Sigurdsson and Gudmundsson (1956) of cases in the Akureyri outbreak of 1948–49 (Sigurdsson et al. 1950); of 39 patients examined only 12 (31%) were free from objective clinical signs, and only 5 (13%) considered themselves completely recovered. Pareses, persistent sensory impairment, muscle tenderness, and proneness to fatigue are features common to both our series. Sigurdsson and Gudmundsson (1956), however, record atrophy of muscle in 6 cases, a feature which was not observed in our series.

Galpine and Brady (1957) report 7 cases in 1956 in Coventry, where the disease was also observed in the summer of 1953; 1 woman, aged 22, developed in 1956 an illness which was strikingly similar to what she had experienced in 1953; she had been quite well in the intervening period, and this might therefore be regarded as a case of fresh infection rather than a relapse. In our own series 1 patient has recently developed symptoms similar to those she exhibited twelve months previously, posing the problem of a fresh infection or a relapse. Several patients have reported a recrudescence of symptoms after an ordinary cold. During 1957 we treated 12 cases of this type of infection; the disease may therefore be regarded as endemic. Pareses and exaggerated tendon-reflexes without muscle wasting, sensory impairment which persists, normal or near normal C.S.F., negative virological and serological investigations, sequelæ suggesting cortical or even extrapyramidal damage, and finally an electromyogram which, though revealing an unexplained lesion, shows no evidence of destruction of the neurone, all indicate a now world-wide infection of the central nervous system of unknown ætiology, capable of manifesting in acute epidemic episodes, which is certainly not a form of poliomyelitis although in its initial stages it may be readily confused with poliomyelitis and, in its aftermath, with hysteria.

Summary

The symptoms and physical signs of 34 cases of acute encephalomyelitis in North West London in 1955 and 1956 are described.

In its early stages this disease resembles poliomyelitis, and in its later stages hysteria.

The ætiological agent remains unknown, but the persistence of what must now be regarded as an endemic infection demands a more general recognition of the syndrome and earlier virological and serological investigation.

Although a negative finding does not exclude the disease, electromyography provides a valuable diagnostic test, particularly in the differentiation from poliomyelitis.

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FAMILIAL HYPERGAMMAGLOBULINÆMIA AND SYSTEMIC LUPUS ERYTHEMATOSUS

TORE LEONHARDT
M.D.

From Malmö General Hospital, Sweden

THE ætiology and pathogenesis of systemic (disseminated) lupus erythematosus (S.L.E.), like those of other collagen diseases, are obscure and have given rise to much speculation. Suggested causes include infections, endocrine factors, allergy, and hypersensitivity (Harvey et al. 1954) and "constitutional factors" (Baehr 1956). The predisposing importance of sex and age is well known.

Reports of the familial occurrence of S.L.E. might argue for an inherited disposition, but such reports are few (table I). The familial occurrence of chronic discoid lupus erythematosus, on the other hand, has long been known. Since many workers regard this condition as allied to S.L.E. (Allende 1956), such reports also deserve attention. About 40 cases have been described in 1901–55. In a few of them systemic involvement may be assumed (table I).

Hypergammaglobulinæmia is an almost regular feature of S.L.E., as of many other collagen diseases (Hansen 1954). The gammaglobulin fraction contains various antibodies (Enders 1944) as well as the L.E. cell factor (Haserick 1950, Haserick and Lewis 1950). The real significance of hypergammaglobulinæmia in collagen diseases is not understood.

Inherited agammaglobulinæmia with decreased capacity to develop gammaglobulins is now a well-recognised disease (Kulneff et al. 1955, Porter 1955, and others). Hypergammaglobulinæmia has occasionally been observed in relations of patients with agammaglobulinæmia (Young et al. 1955, Good and Zak 1956). Otherwise the existence of an inherited form of hypergammaglobulinæmia seems not to have been recognised yet; so I report here a striking example of hypergammaglobulinæmia and S.L.E. in at least 3 of 14 siblings.

Material and Methods

2 of the siblings were treated for S.L.E. in Malmö General Hospital and 1 was treated in Hälsingborg General Hospital. The 11 other siblings were examined for their electrophoretic serum-protein patterns. Of the 5 siblings then found to have serum-gammaglobulin levels above 1·30 g. per 100 ml. 4 were investigated more closely: general clinical examination, routine blood studies and analysis of urine, thorough serological investigation, search for L.E. cells in peripheral blood, and radiography of chest and nasal sinuses. The 5th (case 4), a female, lives in Canada, but valuable information about her general condition was supplied by her family physician, and some laboratory tests were made at the Hospital for Sick Children, Toronto.

The serum-proteins were analysed electrophoretically by the filter-paper method described by Laurell et al. (1956). In case 4 a filter-paper preparation of serum was obtained from Canada and then coloured and eluted in our laboratory. In case 1 the serum-proteins had been analysed by free electrophoresis in 1951 in the Clinical Chemistry Laboratory, Lund.

The normal values for serum electrophoresis on paper used in our laboratory are based on data from 85 healthy blood-donors. The limits of the normal range are calculated from the mean value ± 2 S.D.

In our laboratory Zimmer's two-hour blood-clot technique, modified by Hargraves, is preferred for demonstrating L.E. cells (Hargraves 1954). In case 4, in which a L.E. cell preparation was made in Toronto, whole blood was defibrinated by shaking with glass beads for 10 minutes. The blood was next incubated for two hours at 37°C and a smear was made from the buffy coat.

Case-reports

Case 1.—A woman, aged 47, was admitted to the Hälsingborg General Hospital on Aug. 30, 1951, with four or five years' history of Raynaud's disease of her fingers, about four years' history of a rash on her face, and two years' history of dyspnœa.

On examination she was thin and had dyspnœa at rest, butterfly erythema, and cyanotic fingers, with signs of cor pulmonale and pericarditis. Her erythrocyte-sedimentation rate (E.S.R.) was 100–130 mm. in 1 hr. (Westergren), her electrophoretic serum-protein pattern was altered (table II), and she had moderate anæmia (hæmoglobin 9·6–12·1 g. per 100 ml., red cells 2,700,000–3,700,000 per c.mm.), a normal white-cell count, and proteinuria. L.E. cells were found in her sternal marrow.

Course.—The patient's condition deteriorated rapidly, and penicillin therapy did not control her increasing pyrexia. She died on Sept. 27, 1951. Necropsy showed pericarditis and pleuritis, extensive interstitial lesions of the lungs, small interstitial round-cell infiltrations and fibrinoid deposits in the myocardium, and a few wire-loop lesions of the kidneys.

TABLE I—PREVIOUS REPORTS OF FAMILIAL OCCURRENCE OF SYSTEMIC AND CHRONIC DISCOID LUPUS ERYTHEMATOSUS

Reference	Sex	Age (yr.)	Relationship	Form of lupus erythematosus	Remarks
Legobbe (1937)	F	21	Third cousins	Cutaneous	Systemic involvement highly probable
	F	33		"	Systemic involvement highly probable
Rabeau and Ukrainczyk (1939)	F	50	Mother and daughter	"	Some symptoms and signs suggesting systemic involvement
	F	25		"	Probably no systemic involvement
Davis and Gutridge (1951)	F	18	Monovular twins	Systemic	Typical symptoms and course
	F	20		"	Necropsy
Pirofsky and Shearn (1953)	F	36	Mother and son	"	"
	M	17		"	"
Adams (1954)	F	41	Mother and daughter	"	Not diagnosed during life; symptoms and necropsy highly suggestive
	F	30		"	Symptoms, course, L.E. cells
McCuistion and Schoch (1954)	F	38	Mother and son	"	Symptoms, L.E. cells
	M	0		Cutaneous	Reversible; no signs of systemic involvement
Grupper and David (1955)	F	58	Mother and son	Cutaneous*	Many symptoms and signs suggesting systemic involvement
	M	30		Cutaneous*	" " " " "
Glagov and Gechman (1956)	F	44	Mother and daughter	Systemic	Symptoms, course, L.E. cells
	F	18		"	Necropsy

* "L.E. discoïde disséminé."

TABLE II—ELECTROPHORETIC PROTEIN PATTERNS IN 14 SIBLINGS

Sibling no.	Date	Total protein	Albumin	Alpha-1	Alpha-2	Beta-1+2	Gamma
Normal range (g. per 100 ml.)		6·6–7·7	4·2–5·0	0·27–0·42	0·40–0·63	0·64–1·02	0·65–1·11*
1	Sept., 1956	7·5	4·68	0·34	0·48	0·83	1·17
2	Sept., 1956	7·6	4·69	0·30	0·48	0·76	1·37
3	Aug., 1956	7·2	4·34	0·31	0·48	0·70	1·37
4	Sept., 1951	7·0	2·3†	..	0·32	0·61	3·8
5	Aug., 1956	7·9	4·81	0·38	0·50	0·84	1·37
6	Sept., 1956	7·3	4·71	0·29	0·46	0·73	1·11
7	Sept., 1956	7·6	4·70	0·30	0·50	0·64	1·46
8	Aug., 1956	7·3	4·49	0·34	0·59	0·74	1·14
9	Sept., 1956	7·2	4·76	0·26	0·40	0·65	1·13
10	April, 1955	9·0	2·82	0·32	0·64	0·81	4·41
	July, 1956	6·5	2·03	0·36	0·58	0·59	2·93
11	July, 1954	6·9	3·62	0·28	0·46	0·60	1·94
	Sept., 1956	7·9	4·07	0·32	0·58	0·66	2·27
12‡	Sept., 1956	6·6	3·69	0·36	0·63	0·82	1·10
13	Oct., 1956	9·8	4·76	0·24	0·45	0·57	3·78
14	Aug., 1956	7·2	4·58	0·36	0·55	0·74	0·94

* Mean value 0·89.
† Albumin + alpha-1 globulin (free electrophoresis).
‡ This woman was delivered 10 days before serum sample was taken, which explains low albumin and rather high alpha-2 globulin values.

The patient was sensitive to sunshine and had been treated with penicillin in September, 1951.

Case 2.—A younger sister, aged 21, developed in 1939 chronic purpura of her legs with a raised E.S.R. (72–140 mm. in 1 hr. in 1940–45) and serum-protein changes (in 1943 the albumin was 4·0 g. per 100 ml. and the globulin 6·2 g. per 100 ml.). On examination at this hospital her disease was diagnosed as purpura hyperglobulinæmia, and the case was published by Waldenström (1952).

Attack of S.L.E.—Later, arthralgia developed and gradually progressed despite the absence of significant joint changes. A course of cortisone in February, 1952, had a temporary beneficial effect on the joint pain but not on the purpura or on a recent urticaria. From July, 1953, cortisone was given continuously. In June, 1954, treatment with phenylbutazone and penicillin was followed by a severe illness, with high pyrexia, azotæmia, general exanthema with typical butterfly lesion, and numerous L.E. cells in the peripheral blood. Both remedies were stopped, and the pyrexia subsided.

Course.—After this attack of acute S.L.E. the patient's general condition gradually deteriorated. Continuous steroid hormone therapy (cortisone, prednisone) did not prevent the disease from progressing. The patient had pronounced fatigue, dyspnœa, bouts of pyrexia, pleuritic pain, arthralgia, and myalgia. In July, 1955, a week's course of phenylbutazone was again followed by pyrexia, stomatitis, and dermatitis. Repeated laboratory studies showed normochromic anæmia of varying severity, leucopenia (1500–3000 per c.mm.), a raised E.S.R., serum-protein changes (table II), L.E. cells in peripheral blood on several occasions, and proteinuria. On April 6, 1957, the patient died from a severe exacerbation at the age of 39.

Necropsy showed interstitial leucocytic infiltration of the myocardium, fatty degeneration and necrosis of the liver, pronounced periarterial fibrosis of the spleen, swollen endothelial cells of the lymph-nodes, thickening of the glomerular capillary loops (but no wire-loop lesions), and moderate chronic pyelonephritis.

The patient had been treated with sulphonamides (April, 1942), amidopyrine (October, 1945), penicillin (April, 1952, April–July, 1954), streptomycin (July, 1954), and phenylbutazone (June–July, 1954, July, 1955).

Case 3.—The female heterologous twin of case 2 was admitted to hospital because of abdominal pain in 1935, when her E.S.R. was found to be 70–118 in 1 hr. She had recurrent attacks of colic and in 1942 underwent cholecystectomy. Subsequently her E.S.R. was 32–83 mm. in 1 hr. Butterfly erythema was first seen in the summer of 1951. She also had slight anæmia (hæmoglobin 9·8 g. per 100 ml. and red cells 3,000,000 per c.mm.), fairly low white-cell and platelet counts (4400 and 128,000 per c.mm. respectively), serum-protein changes (albumin 4·35 g. and globulin 4·3 g. per 100 ml.), and serological abnormalities (anticomplementary titre 80, antistreptolysin titre 500, and agglutination of sensitised sheep erythrocytes 1/40). S.L.E. was diagnosed. The patient received corticotrophin to a total of 350 units, and some weeks later the facial erythema disappeared, only to recur with red patches on other regions of the body exposed to sunlight. In 1953 mild arthralgia appeared and the patient complained of spells of pronounced fatigue.

Readmission.—In the summer of 1954 she was readmitted to hospital. Her disease was then quiescent and the butterfly erythema barely discernible. The E.S.R. was 45–60 mm. in 1 hr., hæmoglobin 12·2 g. per 100 ml., red cells 3,700,000 per c.mm., white cells 3900–5200 per c.mm., and serum-proteins as shown in table II. No L.E. cells were found in her peripheral blood.

Follow-up.—Re-examined as an outpatient in September, 1956, she revealed no further change in her condition.

The patient was sensitive to sunshine and had been treated with penicillin in May, 1954.

Case 4.—Another sister, born in 1923, had gonorrhœa in 1942 and was admitted to hospitals in Stockholm in 1943, 1944, and 1947 with salpingo-oöphoritis, in 1948 with dysmenorrhœa and sterility (when laparotomy was done and adhesions were removed), and in 1949 with a ruptured tubal pregnancy. In 1944 she underwent cholecystectomy for gallstones. During those years her E.S.R. varied between 60 and 132 mm. in 1 hr. and was high even during the absence of other signs of acute inflammation.

Afterwards the patient emigrated to Canada. She was operated on there in June, 1956, for uterine prolapse. Apart from this occasion she had not been in hospital, though she had sought medical advice for undue fatigue and slight arthralgia of her shoulders and arms. When last seen she was in a good general condition and showed no sign of acute disease. Laboratory studies in October, 1956, showed hæmoglobin 12·0 g. per 100 ml., red cells 4,100,000 per c.mm., white cells 5300 per c.mm., E.S.R. 99 mm. in 1 hr. (Westergren), cephalin-cholesterol flocculation ++++, thymol turbidity 10 MacLagan units, thymol flocculation +.+++, serum-alkaline phosphatase activity 4·4 King-Armstrong units, and serum-bilirubin level normal. Electrophoresis revealed a striking disturbance of the serum-proteins (table II). No L.E. cells were found in her peripheral blood.

The patient had been treated with penicillin in October, 1949.

Of the remaining 10 siblings, no. 1, a woman aged 58, had been treated in hospital for gallstones and had obesity and hypertension; no. 3, a woman aged 54, had had tuberculous lesions, sometimes suppurative, of the cervical and axillary lymph-nodes from childhood until the age of 47, but no signs of activity since then and no sign of disease on radiography of her chest; no. 7, a woman aged 45, had tuberculous lesions of her cervical lymph-nodes in childhood but had otherwise been healthy; and nos. 2, 5, 6, 8, 9, 12, and 14 had always felt well. Examination of siblings nos. 2, 3, 5, and 7 (who had gammaglobulin fractions exceeding 1·30 g. per 100 ml.) revealed nothing of relevant interest.

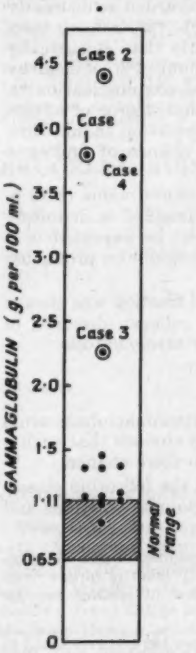

Fig. 1—Serum gammaglobulin levels in 14 siblings. Ringed plotting points represent cases of S.L.E.

Results of Electrophoresis

The results of electrophoresis of the serum-proteins are presented in table II. The distribution of the gamma-globulin values in relation to the normal range is illustrated in fig. 1. The normal values given in table II and in fig. 1 differ somewhat from those usually published.

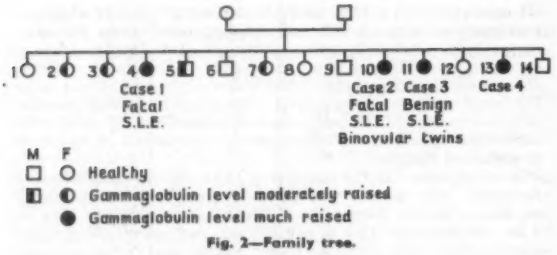

Fig. 2—Family tree.

The mean gammaglobulin value of 0·89 g. per 100 ml. and the upper limit of 1·11 g. per 100 ml. are thus lower than the corresponding values used in several other laboratories.

In the 3 cases of S.L.E. the electrophoretic serum-protein patterns showed the typical changes: decreased albumin and increased gammaglobulin fractions (Coburn and Moore 1943, Walker and Benditt 1950, and others). In case 2 the alpha-2 globulin was sometimes increased, a non-specific change seen in the acute stage.

The gammaglobulin fraction was increased in most of the other siblings too: 6 of them (nos. 1, 6, 8, 9, 12, and 14) had values between 0·94 and 1·17 g. per 100 ml. Only 2·3% of healthy people should have a gammaglobulin value of 1·11 g. per 100 ml. or more, because this value corresponds to a deviation from the mean of 2 S.D. However, too much attention should not be attached to single results slightly deviating from this limit. Yet values ranging from 0·94 to 1·17 g. per 100 ml. in 6 siblings were of interest because they were on a definitely higher level than what might be expected in 6 persons selected at random from a healthy population.

In 4 of the siblings (nos. 2, 3, 5, and 7) the gammaglobulin fractions ranged between 1·37 and 1·46 g. per 100 ml. Gammaglobulin values exceeding the arbitrarily chosen limit of 1·30 g. per 100 ml., corresponding to a deviation from the mean of 3·7 S.D., might be regarded as distinctly pathological. In our laboratory such values have been encountered somewhat more frequently than statistically expected, but not in more than about 2% of healthy blood-donors (B. F. Nosslin, personal communication *). The chance of finding 2 cases with that degree of hypergammaglobulinæmia in a healthy population should then be something like $(2/100)^2$ and the chance of finding 4 cases $(2/100)^4$ or almost negligible.

In 1 sibling (no. 13) the gammaglobulin value (3·78 g. per 100 ml.) was high enough to be classified as definitely pathological. Such a value could not be expected in a healthy person but suggests a gammaglobulin-producing (collagen) disease.

The increase of the gammaglobulin fraction was always of the broad type, as in virus and collagen diseases, in contrast to the narrow type seen in myelomatosis.

Discussion

In this family of 14 siblings hypergammaglobulinæmia was strikingly frequent (fig. 2). It is obvious that such a distribution could not be ascribed to mere chance.

The siblings could be divided into the following classes according to the size of the gammaglobulin fractions and the clinical condition:

(1) Normal or slightly increased gammaglobulin fraction (below 1·30 g. per 100 ml.). Subjectively healthy (apart from symptoms of obesity and hypertension in sibling no. 1). Siblings nos. 1, 6, 8, 9, 12, and 14.

(2) Gammaglobulin fraction distinctly pathologically increased (more than 1·30 g. per 100 ml.). Clinically healthy and no L.E. cells. Siblings nos. 2, 3, 5, and 7.

(3) Gammaglobulin fraction greatly pathologically increased. Only slight symptoms. Abnormal serum-protein reactions but no signs of active disease. No L.E. cells. This condition (sibling no. 13) corresponds to what has been called "essential hyperglobulinæmia" by Waldenström (1944, 1954).

(4) Gammaglobulin fraction greatly pathologically increased. Typical butterfly erythema and other symptoms and signs but no L.E. cells. S.L.E. of benign course. Sibling no. 11.

(5) Gammaglobulin fraction greatly pathologically increased. L.E. cells in sternal marrow (sibling no. 4) or in peripheral blood (sibling no. 10). Clear-cut S.L.E. of unfavourable course.

The present cases suggest that hypergammaglobulinæmia may precede the other manifestations of S.L.E. In case 3 the E.S.R. was known to have been high for at least fifteen years before the appearance of the other symptoms and the establishment of S.L.E. A chronically high E.S.R. is usually due to an increase of gammaglobulin (Malmros and Blix 1946, Olhagen and Liljestrand 1955). In case 2 the disease consisted for many years of an apparently benign form of chronic purpura with high E.S.R. and increased serum-globulins—purpura hyperglobulinæmica of Waldenström (1948). Arthritic symptoms gradually became more pronounced, and finally a full-blown S.L.E. developed. Case 4, who had a decidedly pathological increase of gammaglobulin but no other signs of active disease, had had an unexplained high E.S.R. for at least fourteen years. In many of the other siblings the E.S.R. had also been high on earlier occasions, indicating that their hypergammaglobulinæmia was not temporary (see table III).

By careful history-taking in cases of S.L.E. it is possible to establish that the acute illness may be preceded for many years by symptoms such as arthralgia or skin lesions (Dubois 1953, 1956) and signs such as a false positive serological test for syphilis (Haserick and Long 1952).

TABLE III—E.S.R. AND GAMMAGLOBULIN VALUES IN 14 SIBLINGS

Sibling no.	Case no.	Year of birth	Sex	Year of examination	E.S.R. (mm. per 1 hr.)	Gammaglobulin (g. per 100 ml.)	Clinical condition
1		1898	F	1953	11	..	Obesity, hypertension
				1956	37	1·17	Obesity, hypertension
2		1900	F	1953	25	..	Healthy
				1956	21	1·37	Healthy
3		1902	F	1931	68	..	Tuberculous lymphadenitis
				1953	24	..	Healthy
				1956	29	1·37	Healthy
4	1	1904	F	1951	130	3·8	Acute fatal S.L.E.
5		1906	M	1953	11	..	Healthy
				1956	17	1·37	Healthy
6		1908	M	1953	6	..	Healthy
				1956	8	1·11	Healthy
7		1911	F	1953	14	..	Healthy
				1956	16	1·46	Healthy
8		1913	F	1953	8	..	Healthy
				1956	14	1·14	Healthy
9		1915	M	1953	5	..	Healthy
				1956	8	1·13	Healthy
10*	2	1918	F	1940	80	..	Purpura, not specified
				1943	92	(6·2)	Purpura, not specified
				1951	126	(6·3)	Purpura hyperglobulinæmia
				1955	127	4·41	S.L.E., unfavourable course
				1956	116	2·93	S.L.E., unfavourable course
11*	3	1918	F	1935	118	..	Abdominal pain
				1951	74	(4·3)	S.L.E., benign course
				1954	80	1·94	S.L.E., benign course
				1956	70	2·27	S.L.E., benign course
12		1920	F	1953	43	..	Healthy
				1956	10	1·10	Healthy
13	4	1923	F	1943	120	..	Salpingitis
				1956	99	3·78	Healthy
14		1925	M	1954	4	..	Healthy
				1956	6	0·94	Healthy

Numerals in parentheses indicate globulin value determined by a salting-out method.
* Heterologous twins.

* Gammaglobulin values exceeding 1·30 g. per 100 ml. were found in 19 (1·6%) of 1184 males and in 6 (2·5%) of 238 females. The highest values were 1·86 g. per 100 ml. in a male and 1·54 g. per 100 ml. in a female. Naturally it may be doubted whether all of these persons were healthy in the strict sense of the word.

Thus it may be difficult to determine the onset of S.L.E. (Harvey et al. 1954). In the present family, hypergammaglobulinæmia seems to be a basic abnormality. In some cases first slight, then severe symptoms and signs of active disease supervened. If these were many or characteristic enough (butterfly erythema, L.E. cell phenomenon, anæmia, leucopenia, renal involvement), the cases were classified as S.L.E.

The familial occurrence of S.L.E. and hypergammaglobulinæmia (as a precursor of S.L.E.) might be explained by common environmental factors (Neuss 1955) or by heredity.

The possibility of an infectious (virus ?) disease must be considered. There is, however, but little evidence in support of the theory that S.L.E. is caused by micro-organisms (Cluxton and Krause 1943, Harvey et al. 1954). The placental transmission of antigens or of sensitising antibodies may also be referred to environmental factors and is by some workers (Glagov and Gechman 1956) thought to explain the familial occurrence of S.L.E. It seems strange, however, that placental factors should not lead to manifest disease until adult age. Finally, various antigens met with during postnatal life might be common environmental factors. S.L.E. is often thought to be a hypersensitivity disease, and it is in any case well documented that the onset or an exacerbation of it is often preceded by drug treatment (Fox 1943, Gold 1951, Berk 1957). Yet it appears likely that only persons with the appropriate constitutional type (Honey 1956) develop S.L.E. (or hypergammaglobulinæmia) when exposed to unfavourable antigens.

An inherited disposition therefore remains a possibility and may be the most important factor. The possible mode of inheritance in the present family cannot be discussed until other members of it have been examined. About the nature of the inherited disposition only tentative suggestions can be made.

The power to form gammaglobulins presumably varies from one person to another and is sometimes hereditarily determined. In hereditary agammaglobulinæmia the formation of gammaglobulin is deficient. One can imagine the opposite of this condition : an inherited disposition to overproduction of gammaglobulin—an abnormal readiness of the reticulo-endothelial system and plasma-cells to develop antibodies of different types. The degree of the resultant hypergammaglobulinæmia might be related to the amount and type of antigens met with during life. Some antigens might incite the production of injurious antibodies or even auto-antibodies. Mesenchymal structures of various organs might then be affected and collagen disease result (Teilum 1938, Ehrich 1952, Gold 1953).

The mechanism suggested might explain why the degree of hypergammaglobulinæmia varied so widely from one sibling to another in the present family, and why only 3 siblings had manifest S.L.E. The deleterious effect of a supposed antigen was observed in case 2, where the patient's apparently benign disease (purpura hyperglobulinæmica) changed to severe typical S.L.E. after treatment with phenylbutazone, to which the patient became hypersensitive (cf. Berk 1957).

Summary

Hypergammaglobulinæmia and S.L.E. were strikingly frequent in a family of 14 siblings : 3 of them had S.L.E. with high gammaglobulin values ; and 1 had a decidedly pathological increase of gammaglobulin without other symptoms of active disease.

4 other siblings had distinctly pathological increases of gammaglobulin but were clinically healthy.

The remaining 6 had normal or slightly increased gammaglobulin values and were on the whole healthy.

That hypergammaglobulinæmia may precede other symptoms of S.L.E. is suggested by some observations in the case-reports.

It is suggested that there may be an inherited tendency to overproduction of gammaglobulin, leading to hypergammaglobulinæmia and sometimes S.L.E. The development of S.L.E. might be provoked by unfavourable antigens. The deleterious effect of a presumed antigen was observed in 1 of the siblings with S.L.E., who became hypersensitive to phenylbutazone.

I wish to thank Dr. K. Liedholm, head of the medical department of Hälsingborg General Hospital, for permission to publish case 1 ; Dr. J. Rekai, of Toronto, for valuable information about case 4 ; and Dr. A. Sass-Kortsak, at the Hospital for Sick Children, Toronto, for laboratory investigations in the same case.

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BRUCELLA SUIS INFECTION OF A CHILD IN EIRE

T. PEARSE WILLIAMS
M.D. Lond., F.R.C.P.
PHYSICIAN

D. M. ENTWISTLE *
M.B. Lond.
HOUSE-PHYSICIAN

P. L. MASTERS
M.D. Lond., D.C.H.
PATHOLOGIST

A. C. WOODS †
F.I.M.L.T.

PADDINGTON GREEN CHILDREN'S HOSPITAL, LONDON

THIS is the first report of human infection by *Brucella suis* (American type) in the British Isles. Infection of cattle by *Br. abortus* is endemic to these islands, and human infection is sporadic. *Br. melitensis* has been isolated from cattle and from their milk in various parts of Great Britain since 1940, but it has not been isolated from man in Britain (Cruickshank 1954). *Br. suis* has

* Now at the Royal Victoria Hospital, Folkestone.
† Now at the Department of Hæmatology, Brompton Hospital.

not been reported to infect livestock or man in Great Britain (Wilson and Miles 1955) or in Eire. It has been found mainly in the Middle-West of North America, Brazil, and Argentina, where it infects both pigs and cattle. The nearest isolation that has come to our notice is from Switzerland, where there have been a few isolations of *Br. suis* from pigs and Dr. W. Sackmann isolated a *Br. suis* (American type) from the milk of a cow (D. J. H. Payne, personal communication).

Human infection by *Br. suis* is liable to be more severe and more common in childhood than infection by *Br. abortus* (Wilson and Miles 1955). If infection of livestock by *Br. suis* should become established in the British Isles, the consequences for agriculture and for public health might be serious.

Case-report

A boy, aged 4 years, developed listlessness, loss of appetite, and fever about the middle of August, 1956, while staying on a farm in Eire. After three weeks' illness he was admitted to hospital. The only physical signs on admission were slight enlargement of his spleen and occipital and posterior cervical lymph-nodes. The fever settled rapidly, and he was discharged a week later. At the end of September he returned to his home in London and was admitted to hospital two days later with a recurrence of his original symptoms.

On admission his temperature was 99°F. His spleen was just palpable, and he had generalised slight enlargement of his superficial lymph-nodes, hæmoglobin 10·8 g. per 100 ml., apparently normal red cells in the film; erythrocyte-sedimentation rate (E.S.R.) 9 mm. in 1 hr. (Westergren: 100 mm. column); and white-cell count 4600 (polymorphs 2200) per c.mm.; no atypical large mononuclear cells. Radiography of his chest and laboratory examinations of his urine and stools gave normal results. The Paul-Bunnell and Widal tests were negative, but agglutination against *Br. abortus* was positive to a titre of 1 in 1280.

Treatment and Progress.—During his first ten days in hospital he had a temperature of 100–101°F on alternate evenings. A blood-culture taken on the ninth day after admission yielded a gram-negative coccobacillus later identified as *Br. suis*. A suspension of the isolated organism agglutinated in a dilution of the patient's serum of 1 in 1280. After he had been in hospital two weeks his fever was still increasing and reached 102·2°F in the evening. Aureomycin 0·25 g. six-hourly, was given for a fortnight. The fever became more continuous during the first three days of the course but the boy's temperature fell rapidly to normal on the fourth day. A similar response to aureomycin was noted by Spink (1956).

Follow-up.—There had been no recurrence of symptoms when the boy was seen three months later.

Bacteriology

The organism was grown from two blood-culture bottles, each containing 50 ml. of glucose broth and 2 ml. of blood, after incubation for three and four days respectively. Subcultures were made to blood-agar, boiled blood-agar, and liver-infusion agar and incubated at 37°C aerobically with added carbon dioxide. Tiny colonies were visible on all three media after two days. The organism was a small gram-negative coccobacillus, formed a smooth suspension in saline solution, and was agglutinated rapidly on a slide by *Br. abortus* antiserum. The following features led us to believe that it was *Brucella suis* (American type):

(1) Carbon dioxide was unnecessary for good growth.

(2) Hydrogen sulphide was still being produced after five days' growth on liver-infusion agar.

(3) Growth took place on liver-infusion agar containing thionin 1 in 60,000 but not on the same medium containing basic fuchsin 1 in 50,000, methyl violet 1 in 100,000, or pyronin 1 in 30,000.

A culture was sent to Dr. D. J. H. Payne, reference bacteriologist for the brucellæ in the Public Health Laboratory Service. He confirmed the above findings and added the following:

(4) Agglutination test with monospecific sera: titre with *Br. abortus* antiserum 1 in 8 (traces at 1 in 16); titre with *Br. melitensis* antiserum nil.

(5) High urease activity similar to control strain of *Br. suis*. Control strains of *Br. abortus* and *melitensis* show weak urease activity.

Epidemiology

The patient's mother, his sisters (aged 3 years and 1 year and 11 months), and his brother (aged 8 months) stayed on the farm for two months. The patient had been there for two to three weeks, when he became unwell. There were cows on the farm, and all the family drank unheated milk from them. The father was on the farm for a week and milked cows while he was there. The pigs on the farm were home-reared, and there was no known contact between them and the family. Investigations of the pigs and cows on the farm by the veterinary authorities have so far proved negative.

An E.S.R. and serum agglutinins to *Br. abortus* and *Br. suis* (patient's strain) were determined for each member of the family. None of the sera showed agglutinins at titres of 1 in 20 to 1 in 2560 and the E.S.R.s were less than 8 mm. after 1 hour (Westergren: 100 mm. column), except for the sister aged 3 years. Her E.S.R. was 17 mm. but had dropped to 4 mm. five weeks later.

The principal ways of infecting man with any of the three types of brucellæ are (1) direct contact with infected animals or their secretions, with entry through the skin, and (2) the drinking of raw milk from infected animals (Spink 1956). Either method of infection was possible in this case. Garrod (1939) found *Br. abortus* and *Br. melitensis* particularly susceptible to the bactericidal action of gastric juice and suggested that this is partly responsible for the low incidence of infection in people drinking milk containing brucellæ. His further suggestion that achlorhydria predisposes to milkborne infection by brucellæ led us to give our patient an alcohol and histamine test-meal. This showed more than the average concentration of free acid in all the specimens.

We wish to thank Prof. Robert Cruickshank and Dr. Donald Payne for their interest and advice.

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New Inventions

AN AID IN THE REDUCTION OF RADIATION HAZARD IN THE OPERATING-THEATRE

MANY technical advances have been made in nailing operations on the neck of the femur, not least in the matter of radiographic control, but it is still not uncommon practice for the film cassette to be held in position by hand while the lateral film is being taken. The dangers to the hands from direct rays and to other parts of the body from "scatter" have been vividly described by Watson-Jones,[1] but one still sees theatre sisters, house-surgeons, and anæsthetists, as well as the operating surgeon, exposing themselves to radiation in this way.

This difficulty of the anteroposterior films was solved over 20 years ago by the introduction of a cassette-holder, designed by Mr. R. M. Leman, superintendent radiographer, Royal Victoria Hospital, Belfast. This appliance has for many years fulfilled the purposes for which it was designed, and similar devices are in use in many hospitals. It seemed to me that a simple modification of this equipment would suffice to counteract the dangers associated with lateral pictures. Such a modification has now been made, tried out, and found to be effective.

It consists simply of a triangle of wood fitted with a shaft which can be plugged into the upper part of the horizontal cassette-holder. This provides a shelf whose

1. Watson-Jones, R. Fractures and Joint Injuries; vol. I, p. 163. 4th ed., Edinburgh, 1952.

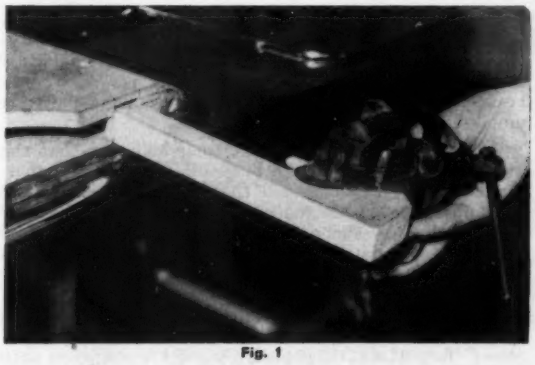

Fig. 1

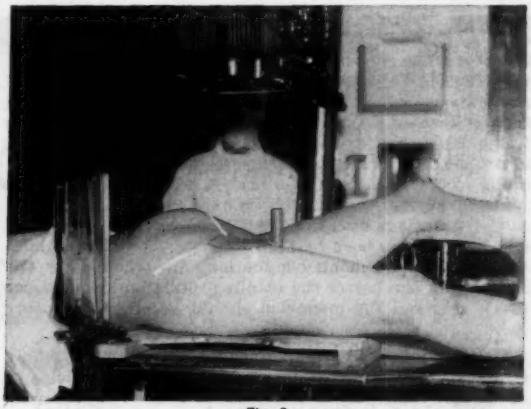

Fig. 2

outer edge makes an angle of 60° with the long axis of the operating-table. To this shelf is clamped a small metal vice which holds the cassette in position for taking the lateral X-ray pictures. The only modification of the vice required is to recess the lower margin of the outer jaw to accommodate the raised edge of the cassette.

The appliance is removable so that it may be fixed to whichever side of the table is required and it need not interfere with moving the patient on to, or off, the operating-table.

Fig. 1 shows how the "shelf" fits the horizontal cassette-holder and fig. 2 shows the apparatus in use.

There are, of course, more complex, probably more efficient, and certainly more expensive devices on the market which mechanically control the position of the lateral film in radiography during hip operations. The present one has the merits of simplicity and cheapness and can easily be adapted to cassette-holders already in use. Not all of the latter will have exactly the same dimensions; so no specifications are given here for the "shelf," beyond stating that its outer edge should lie at 60° to the long axis of the table. This angle is chosen so that the film will lie more or less parallel to the guide wire, which is usually inserted at about 60° to the shaft of the femur. The remaining features of the appliance should be clear from the illustrations.

I am indebted to Mr. W. Rowan, who made the "shelf" for me, and to Mr. R. Wood, for the photographs.

Royal Victoria Hospital, Belfast

J. B. PYPER
M.B. Belf., F.R.C.S.

Medical Societies

ROYAL SOCIETY OF MEDICINE

Stapes Mobilisation

THE section of otology met on Dec. 8, under the presidency of Mr. I. SIMSON HALL, to discuss mobilisation of the stapes and fenestration through its footplate in the treatment of otosclerosis.

Dr. S. ROSEN (New York) pioneered these operations, beginning in 1952 with "indirect mobilisation," in which the footplate fixed by ostosclerotic bone was shifted by pressure on the neck of the stapes with a specially devised instrument. He had found that this operation sometimes left the footplate immobile or led to fractures of the crura, and in 1955 introduced the operation of "direct mobilisation," in which the footplate was attacked directly and pried loose with a sharp-pointed instrument. For patients whose stapes could not be mobilised at all, he made a fenestration in the fossa ovalis—i.e., through the rigid footplate of the stapes—using either a sharp-pointed instrument or one resembling a crochet hook. The operations were done under local anæsthesia, using a microscope and loupe, by an endaural approach reflecting the drum.

Sometimes the crura had to be fractured and the incus removed before the footplate was properly displayed. Fenestration of such a footplate had led to normal and near-normal hearing. Sometimes hearing improved immediately, only to be lost when the drum was replaced but restored by myringotomy.

In 3000 of these operations Dr. Rosen had seen no case of total deafness or facial palsy, and only occasionally slight, transient vertigo after fenestration. Otitis media occasionally complicated the operation and vitiated the result. Of every 10 patients treated (repeatedly if necessary), 7–8 were improved. The operations were not incapacitating and were easy to repeat. The greater the difference between bone-conduction and air-conduction, the greater the indication for stapes operation. Even severe hearing-defects might be improved enough to make a hearing-aid useful. In mixed deafness the stapedial component could be improved. The operation was one for the surgeon experienced in endaural operations, and he recommended practice on 50 fresh cadavers before the operation was attempted on a patient; some poor results might be attributed to lack of such practice. In fenestration the point of the instrument must be felt, as well as seen, to penetrate the footplate.

Helmholtz's concept of conduction of sound through the intact ossicles had been accepted for a hundred years, but Dr. Rosen thought it a sufficient (but not a necessary) condition of good hearing, which he had seen after destruction of the ossicles. In a woman in whom the long process of the incus had been irreversibly dislocated from the stapes, the hearing was still normal after three and a half years. Helmholtz's concept was part of a total phenomenon which was not completely understood.

Mr. TERENCE CAWTHORNE said that these operations on the stapes were slight from the patient's point of view, rarely followed by dizziness, and never as yet by loss of hearing. The results were not yet as good or long-lasting as those of the fenestration operation, but this could be done if the stapes operations failed. In otosclerosis he had often found that the lip of the fenestra ovalis appeared to grip the footplate anteriorly. In indirect mobilisation the force and direction of tug were important; the crura were easily fractured. It might be safer to *push* on the stapes; gouges were indicated in some advanced cases. His results had been almost twice as good with the direct as with the indirect operation. He made an audiogram immediately after mobilisation, with the patient still on the table, and repeated the mobilisation at once if necessary.

Mr. R. S. VENTERS (Carlisle) confessed that, after twenty-five years of temporal-bone surgery, he had practised on no cadaver before his first stapediolysis. He

preferred general anæsthesia, and used spectacles rather than a microscope till the tympanic membrane was reflected. The chorda tympani must be found and pushed medially. It was often hard to find a demarcation between footplate and fenestra, and few patients were suitable for the direct operation. He thought he could determine by palpation in which cases the crura would fracture and in which the operation would succeed. He had had immediate success in 70% of patients, and in 53% the good results persisted for six months or more. He had seen 1 case of transient otitis media and no vertigo; preoperative tinnitus had been relieved. The greater the difference between air and bone conduction, and the flatter the audiogram, the better the results; but there were many exceptions and the operation should be offered to other patients.

Mr. Venters believed that true stapediolysis was rarely achieved, that it was unjustifiable to remove ossicles to make a hole in the footplate, and that mobility was often followed by recurrence or a scar leading to immobility. He thought that often the footplate was immobilised at one end, and at operation the other penetrated the vestibule with a blanket of mucosa, becoming partially mobile.

Dr. ROSEN, replying to the discussion, said that the more operations he did the more often he saw the footplate clearly, and suggested that a surgeon should not start operating on the footplate till he had become used to operating on the neck of the stapes. Under local anæsthesia the patient could sometimes help the surgeon by responding to hearing-tests. In some patients after fenestration the hearing had improved, then deteriorated. In some of these thick adhesions had formed; he assumed that a thin membrane covered the fenestra in the successes. Benefit was delayed longer after fenestration than after any other operation on the stapes.

Reviews of Books

The Epidemiology and Control of Malaria

GEORGE MACDONALD, C.M.G., M.D., F.R.C.P., director of the Ross Institute of Tropical Hygiene. London: Oxford University Press. 1957. Pp. 239. 30*s*.

Professor Macdonald has brought a new approach to the epidemiology of malaria. He has integrated the mathematical analysis of the interaction of numerical factors with the facts found in the field. There is one fundamental difference between him and those who have made this attempt before and who have been thought to have failed. Professor Macdonald accepts the possibility of super-infection, though he does not, of course, insist that it occurs invariably. It may now seem almost bizarre that it was once thought that no man could be reinfected with malaria until he had completely recovered from an initial attack. The wide acceptance of the possibility of such reinfection is due to the work of Professor Macdonald and his colleagues, both at the Ross Institute of Tropical Hygiene and elsewhere; and the book provides a convenient summary of his thesis.

There are chapters on the general aspects: forms of epidemiology, cycles of transmission in man and in the mosquito, quantitative aspects of transmission, "stable" and "unstable" malaria, epidemics, the theory of control. The practical applications are discussed in chapters dealing with malarial survey, insecticides, drugs, and the control programme. A part of the book deals with local features of malaria in the Americas, Europe, and Northern Asia, Africa and Arabia, South and East Asia, and Australasia and the Pacific. Appendices on statistical methods, and such techniques as the detection of resistance against insecticides or their chemical determination, together with a generous index, complete the book.

It will be widely welcomed, not only by epidemiologists but by all whose work brings them in contact with malaria.

The Student Life

The Philosophy of Sir William Osler. Editor: RICHARD E. VERNEY, F.R.C.P.E., physician-in-charge, department of student health, University of Edinburgh. London and Edinburgh: E. & S. Livingstone. 1957. Pp. 214. 15*s*.

THIS anthology of Osler's writings includes such sizable topics as the student of medicine, the qualities required of the physician, the profession of medicine, the clinical years, the collection of a library, and the general practitioner. Four of Osler's biographical studies are included, and as a tailpiece the editor adds his own biography of that remarkable general practitioner, Francis Adams, who practised in Banchory a century ago. Of Adams it was once written: "In any other country such a man would not have been permitted to remain long in such a position. It is . . . something to be both proud and ashamed of, that the most learned physician in Britain, and probably in Europe, is at this moment a country surgeon in a small village on Deeside."

Osler had a singular sympathy with and an intimate understanding of the difficulties and responsibilities of the young student. His advice is every bit as readable and impressive today as when it was written. One thing only has dated—the list of books for a medical student's bedside library (the list compiled by the editor is on a narrower basis). Students of medicine and many in other faculties can hardly fail to profit from a study of Osler's philosophy.

A Theory of Disease

ARTHUR GUIRDHAM, D.M., B.SC., D.P.M. London: Allen & Unwin. 1957. Pp. 204. 21*s*.

MAN has always striven to find some rational and unifying concept of the diseases that assail him. For the savage, the explanation was simple: everything—from apoplexy to the zymotic diseases—could be explained in terms of demoniacal possession. The Greeks postulated degrees of imbalance between the four humours; and later generations invoked malign planetary conjunctions or the Doctrine of Signatures. Successive advances in medical knowledge have since made it harder, rather than easier, to visualise a unitary pattern for disease—though, in our own century, the dawn of bacteriology promised such a pattern to a few, and for a short time.

During many years in practice as a consultant psychiatrist, Dr. Guirdham has tried to formulate a "theory of disease" which will accord with current scientific facts. He concludes that illness is the result of a conflict within the patient between an "undifferentiated and uninterrupted stream of consciousness not imprisoned in a human individuality, and the more individual strata of personality": between, in other words, what has been termed a soul, and a baser self. The level at which the conflict occurs is determined by the moral and religious conditioning of the patient, and this, in turn, he argues, will determine whether the resultant disturbance in health is neurotic, functional, or organic.

Dr. Guirdham's views are obviously based on wide reading about religions, but he also cites modern epidemiological and pharmacological evidence to support them. Few doctors will accept his hypothesis unreservedly, but they will admit the validity of several of his arguments. And even the frankly sceptical will find his digressions on such topics as iatrogenic disease and fashions in disease interesting and salutary reading.

Annotated Bibliography of the History of Medicine in Australia (Sydney: Australian Medical Publishing Co. 1957. Pp. 140. 35*s*.).—Dr. Bryan Gandevia, honorary curator of the medical history museum of the Medical Society of Victoria, has arranged his very useful volume in eighteen sections, with full author and subject indices. Thus the "flying-doctor service" is indexed under "aerial medical service," which gives references to two books and two articles. There are many references to diseases of aborigines and to medical aspects of the transport of convicts. The text is much enriched by the author's short annotations. Every big library should have a copy of this book, which is a great credit to the author and to those who sponsored his work.

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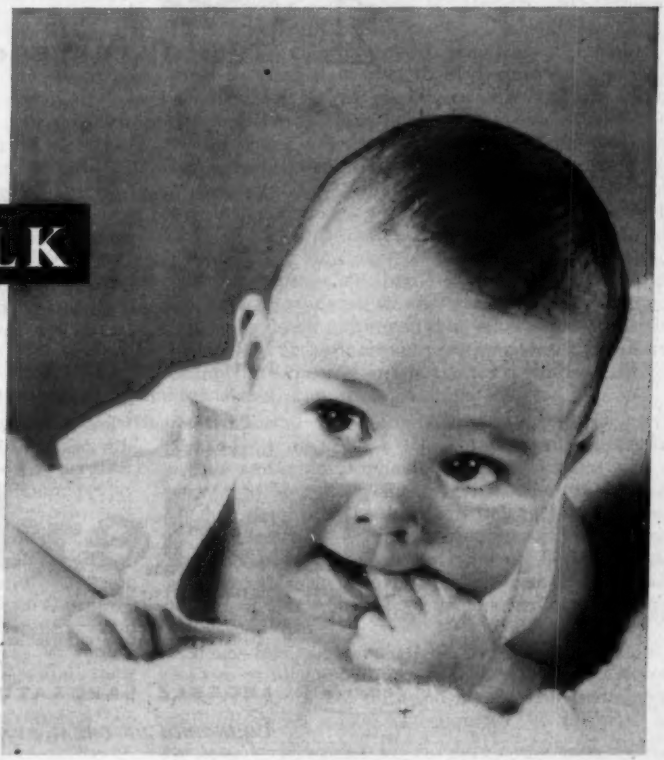

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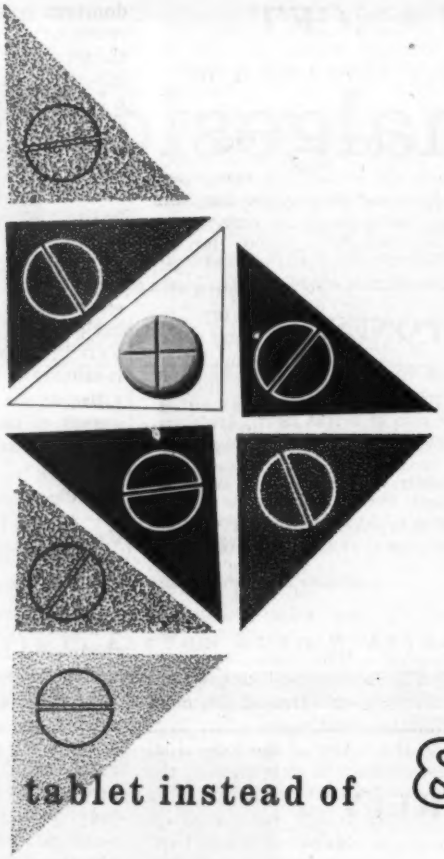

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THE LANCET

LONDON: SATURDAY, DECEMBER 14, 1957

New Combinations of Antibiotics

IT is hard to keep up to date with the many new combinations of antibiotics, and it may be far from easy to assess their value, because the manufacturers sometimes introduce them without adequate laboratory study or clinical trial. We lately evaluated antibiotic combinations,[1] and now JONES and FINLAND [2] report a detailed study of members of the erythromycin group—erythromycin, oleandomycin, and spiramycin—alone and in combination with tetracycline.

With either an agar or a broth-dilution technique they found that, in general, erythromycin was unquestionably superior to oleandomycin or spiramycin in its activity against staphylococci and other gram-positive coccal pathogens. They also showed that oleandomycin was more potent than spiramycin. JONES and FINLAND determined the activity in vitro of combinations of tetracycline with either erythromycin or oleandomycin or spiramycin in various proportions. The combination of tetracycline with erythromycin proved superior to combinations of tetracycline with either oleandomycin or spiramycin; but none of the mixtures, in any of the ratios that were used, was clearly more active than the more potent single component of the mixture on its own. Indeed for most strains the pairs of antibiotics were more often than not found to be inferior to the better of the individual components. JONES and FINLAND determined the antibacterial activity in the plasma of healthy young men after oral administration of the various drugs alone and in combination. The results confirmed their in-vitro findings; none of the combinations showed activity greater than that obtained from the same dose of the more active component of the pair.

The most enthusiastic report of synergism between tetracycline and a member of the erythromycin group was that by ENGLISH et al.,[3] whose claim for enhanced activity of a mixture of 2 parts of tetracycline with 1 part of oleandomycin led to such a combination being marketed under a trade name ('Sigmamycin'). The in-vitro evidence for their claim was not strong, and it is obviously not supported by the work of JONES and FINLAND.[2] In this country GARROD [4] has failed to demonstrate any synergistic activity by such a mixture of tetracycline and oleandomycin against 70 strains of staphylococci; and FAIRBROTHER and SOUTHALL [5] were similarly unable to show synergism, in vitro, against 165 fresh isolates of common pathogens which included 80 strains of *Staphylococcus aureus*. ENGLISH et al.[3] also claimed that this combination in vitro, retarded the emergence of antibiotic-resistant variants of one strain of *Staph. aureus* and one strain of *Streptococcus pyogenes*. To test this claim GARROD [4] habituated six strains and FAIRBROTHER and SOUTHALL [5] three strains of *Staph. aureus* to sigmamycin, oleandomycin, and tetracycline; and their results are in close agreement. Habituation to oleandomycin resulted in the development of considerable resistance to that antibiotic but little or no change in the sensitivity to tetracycline or sigmamycin. Repeated subculture in the presence of tetracycline produced a lesser degree of resistance to the homologous agent and also some increase in resistance to sigmamycin but no change in sensitivity to oleandomycin. Habituation to sigmamycin little changed the sensitivity to oleandomycin; there was some increase in resistance to the combination but this was less than the resulting increase in resistance to tetracycline. GARROD [4] points out that apparently the smaller amount of the weaker antibiotic (oleandomycin) fails to interfere effectively in the reaction of the organism to the major component in the combination (tetracycline). FAIRBROTHER and SOUTHALL [5] consider that these results confirm the claim that the mixture delays, in vitro, the emergence of resistant variants of *Staph. aureus*. JONES and FINLAND [2] noted differences in cross-resistance to erythromycin, oleandomycin, and spiramycin among strains of *Staph. aureus* freshly isolated from patients; whereas complete cross-resistance to all three agents is known to develop in strains repeatedly subcultered in the presence of any one of them. These observations accord with those reported by GARROD [4] and by FAIRBROTHER and SOUTHALL [5]. GARROD referred to cross-resistance as being "double" when resistance involved both erythromycin and oleandomycin, and "dissociated" when it was to one agent only.

It can be concluded only that oleandomycin and spiramycin are so inferior to erythromycin that their adoption for general use is unwarranted; indiscriminate use of these weak erythromycin-like agents may produce a staphylococcal population resistant not only to them but also to erythromycin itself. But when strains of *Staph. aureus* are encountered that are sensitive to these agents but resistant to erythromycin, their use may be justified. Combinations of tetracycline with oleandomycin or spiramycin seem to have little to commend them; for the clinician presenting them may tend not to provide an effective dose of either drug, and he may falsely feel secure because of a mistaken belief that the combination provides better or broader antibacterial activity. There is no evidence whatever that in vivo such combinations delay or prevent the emergence of resistant variants. Furthermore suppression of resistant variants cannot be expected unless the organism is sensitive to both antibiotics in a combination.

JONES and FINLAND [6] have used their in-vivo method to investigate the combination of erythromycin and chloramphenicol. This mixture did not appear to be synergistic. There is some in-vitro evidence [7] that this combination delays the emergence of erythromycin-resistant staphylococci, but there is no proof that the combination has the same action in vivo. It must also be remembered that one component of this combination is a potentially dangerous drug.

Meanwhile, we should seek to exercise restraint in the use of all antibiotics, and particular care to conserve erythromycin for treatment of life-endangering staphylococcal infections acquired in hospital and

1. *Lancet*, July 27, 1957, p. 177.
2. Jones, W. F., Finland, M. *New Engl. J. Med.* 1957, **257**, 481, 536.
3. English, A. R., et al. *Antibiot. Chemother.* 1956, **6**, 511.
4. Garrod, L. P. *Brit. med. J.* July 13, 1957, p. 57.
5. Fairbrother, R. W., Southall, J. E. *Lancet*, Nov. 16, 1957, p. 974.
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7. Wright, S. S., et al. *J. Lab. clin. Med.* 1953, **42**, 877.

thus liable to be resistant to the common antibiotics. If weak erythromycin-like drugs are to be unwisely adopted, we may rely for a time on novobiocin and vancomycin [8]; but how long can the production of genuinely new antibiotics keep us ahead in the downhill race?

"Acute Nephritis"

A FEW years ago Prof. CLIFFORD WILSON and Prof. JEAN HAMBURGER were invited to speak about "nephritis" at a meeting of the Renal Association. In keeping with English usage Professor WILSON spoke about glomerular nephritis. In France, however, the term *néphrite* has wider connotations, and Professor HAMBURGER discussed the classification of all renal diseases. There is nothing new about such a confusion in the nomenclature of renal disease; it is due partly to ignorance of their ætiology.

What is the accepted meaning of the term "acute nephritis"? Does it describe a disease, a syndrome, or certain histological changes? Generally the term is synonymous with a disease—i.e., acute glomerular nephritis, in which infection with hæmolytic streptococci is followed after about two weeks by the sudden onset of hypertension, cardiac failure with œdema, proteinuria, and hæmaturia. The prognosis of this condition is well defined; death occurs in a few days in about 3%, in a few months in 7%, and in a few years in another 10%; the remaining 80% recover completely. In the acute phase the histological changes consist in an intense proliferation and inflammation of the glomerular tufts.

There are other causes of sudden onset of hypertension, cardiac failure with œdema, proteinuria, and hæmaturia—for instance, polyarteritis nodosa, disseminated lupus erythematosus, and anaphylactoid purpura. In these conditions there may be no preceding infection; and, though there are often certain histological similarities to acute glomerular nephritis, the natural history of subsequent events and the prognosis are different. Nevertheless the clinical features of acute glomerular nephritis clearly form a syndrome which may be found in several other disease processes. It would be of help if this syndrome could be defined by some term which does not imply any particular disease; it is only confusing to call it "acute nephritis".

Occasionally the reverse difficulty is evident. Should a condition be called acute nephritis if there is no preceding infection with hæmolytic streptococci, if most of the clinical features of acute glomerular nephritis are absent, and if the histological changes are not those of acute glomerular nephritis? BATES, JENNINGS, and EARLE [9] illustrate this problem in a paper entitled "Acute nephritis unrelated to group A hæmolytic streptococcus infection."

Ten cases are described in which the most prominent clinical feature was hæmaturia; in eight this followed 24–48 hours after the onset of acute pharyngitis, but in two the pharyngitis followed the hæmaturia. No patient had a rise in jugular venous pressure or dyspnœa. Only one patient had pretibial œdema, and two had mild periorbital œdema; there is no mention of diuresis or loss of weight during recovery. Only one patient had a diastolic pressure above 90 mm. Hg. Titres of serum-antibodies against hæmolytic streptococci, including type-specific antibodies against type 12, were measured in all patients, and except for one equivocal response there was no evidence of a preceding streptococcal infection. Renal biopsies were successfully performed in nine patients, but the average interval between the onset of symptoms and the first biopsy was 34 days. This is too long to make a reasonable comparison with the usual case of acute streptococcal glomerular nephritis; in which recovery is rapid. In two patients, however, biopsy was done within 10 days of the onset; at the time of the biopsy one had microscopical hæmaturia but no proteinuria, and the other had gross hæmaturia and some protein in the urine; in the first there were a few minor foci of hypercellularity in the glomerular tufts, and in the second there were no structural abnormalities, though red cells were seen in Bowman's space.

It is clear that these patients did not have the clinical syndrome associated with acute glomerular nephritis, and that they had not recently had an infection with hæmolytic streptococci. In addition, the histological findings in the two cases where biopsy was done near the onset of the hæmaturia were totally different from those which are found in biopsy specimens obtained at a similar time from unselected patients with acute (streptococcal) glomerular nephritis. HUTT, PINNIGER, and DE WARDENER [10] have described the renal-biopsy findings in fourteen cases of acute glomerular nephritis in which the interval between the onset of the disease and the biopsy was 9 days; when proteinuria and hæmaturia were present the characteristic glomerular lesions were found, including proliferation of the cells of the glomerular tufts, œdema and disruption of the basement membrane, and infiltration with polymorph cells.

BATES et al. suspect that in their series the acute pharyngitis was due to a virus infection, and they tentatively suggest that the accompanying hæmaturia was also viral in origin. This seems a very probable explanation, and it is interesting that this is the first time that such a disorder has been described. Whether this condition should be referred to as "acute nephritis" is more debatable.

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Annotations

BENIGN MYALGIC ENCEPHALOMYELITIS

THE onset of benign myalgic encephalomyelitis is commonly insidious with lassitude and malaise, followed by headache and neck stiffness, sometimes with vertigo and vomiting. There may be paræsthesiæ of the face and limbs. Though the patient may shiver, fever is often absent and never severe. Changes in mental state, especially depression and difficulty in concentration, are characteristic, and can easily lead to a diagnosis of hysteria. The patient complains of weakness in a limb or limbs, but total paralysis of a muscle is rare. The muscles are painful, and the pain causes great distress. The patient is generally confined to bed after a few days, though the interval may be as long as several weeks. Physical examination suggests a diffuse disorder of the nervous system, causing cerebral, mid-brain, or spinal lesions. The weakness usually proves to be only slight or moderate, and the reflexes are normal or increased. There is sensory loss, sometimes of glove-and-stocking distribution, sometimes of a bizarre type corresponding to neither segmental nor peripheral-nerve pattern. The muscles hardly ever waste. The cerebrospinal fluid (C.S.F.) is normal. The course of the disease is protracted, often

extending over many months, and relapses are common. But it deserves the description "benign," for it is not a cause of death.

The disease has a strong predilection for females, especially young women, and is best known as an epidemic disorder affecting nurses' homes. Reports of such epidemics have appeared from England,[1–3] Australia,[4] South Africa,[5] and the United States.[6 7] The Royal Free group of hospitals in London experienced a severe outbreak amongst the nurses in 1955,[8] and elsewhere in this issue Dr. Ramsay provides the background to this in an account of sporadic cases outside the hospital but in the same part of London. Probably such cases are arising in many places but are commonly misdiagnosed. In view of the occurrence of sporadic cases the term "epidemic neuromyasthenia," which has been used to describe this disease, seems misleading, and indeed it is doubtful whether "neuromyasthenia" is the appropriate term for the disorder if it is primarily a diffuse affection of the central nervous system.

Attempts to isolate a causal organism have been disappointing. But Shelokov et al.[6] have reported an epidemic in a nurses' home near Washington, D.C., in which the existence of the clinical disease was closely correlated with infection by the Bethesda-Ballerup group of intermediate paracolon organisms. The only well person from whom organisms were isolated and in whom antibodies also developed was a kitchen-girl, first employed about a week before the first clinical case was detected. Two strains of the organism were identified during the epidemic, and the only person in the whole investigation from whom both were isolated was this kitchen-girl. Shelokov et al. conclude that either this organism is responsible for the clinical disease or the unknown causal agent was disseminated with it in contaminated food. In the outbreak at the Royal Free Hospitals the disease seemed to be spread by frequent personal contact,[9] but in any future epidemic special attention must be paid to the possibility that it is food-borne.

Some reports of this disease stress its similarity to poliomyelitis. With so many reports to guide us, the emphasis in the future should be on its points of dissimilarity from poliomyelitis or other neurological disease. Apparently the principal clinical features distinguishing benign myalgic encephalomyelitis are the mental changes (especially depression), the severe muscular pain, the sensory symptoms and signs, the preservation of reflexes, the absence of total paralysis of any muscle, and the normal C.S.F. As Ramsay points out, the electromyograph may be helpful in doubtful cases.

THE DIFFICULT KNEE

ANY surgeon who has done a lot of meniscectomies will know what it is to open a normal knee. To remove a normal cartilage probably does less harm than to overlook a torn one, though there can be little doubt that the joint is damaged by the meniscectomy. Difficulties in diagnosis arise on two occasions—during the clinical examination of the patient and during the operative exploration of the joint. Murdoch[9] has lately reviewed the errors of diagnosis revealed at meniscectomy, and has drawn on an experience of over 2500 operations. With this sort of experience the errors in diagnosis have been reduced to the very low level of 3%, but there can be little doubt that the figure for the whole country is very much higher. The commonest cause of error was the unreliable witness, but surgical mistakes in localisation also played an important part. Tears of the anterior cruciate ligament, recurrent subluxation of the patella, and loose bodies were rarer causes of difficulty.

The problems of meniscectomy are wider than Murdoch's series suggests, since some of the errors of diagnosis may never be revealed by operation. Cartilage injuries are also associated with capsular and ligamentous damage, which can be detected in the recent case only by examination under anæsthesia. Some of the bad results of meniscectomy are undoubtedly caused by overlooking a tear of the cruciate or the medial collateral ligament. Osteochondritis dissecans may often simulate a cartilage injury, and the radiological changes are sometimes late in appearing. Tears of the cartilage may be masked by an associated osteoarthritis, and in these patients meniscectomy often produces dramatic relief. Wiles et al.[10] have commented upon the frequency of chrondromalacia patellæ: and certainly many of the incisions in use for meniscectomy do not allow the surgeon to inspect the patella. Diagnosis of the cartilage lesion in the female is often difficult, and it is wise to bear in mind Smillie's advice[11] that internal derangement of the knee in a woman should be regarded as a recurrent dislocation of the patella until proved otherwise. It is doubtful whether air arthrography, as described by Somerville,[12] is of substantial help in elucidating the difficult lesion. With greater care in clinical examination, and particularly in the examination of recent injuries, the errors in diagnosis can probably be drastically reduced.

SLAUGHTERHOUSES

IN modern abattoirs animals should be killed with the least possible suffering, conditions should be hygienic, and there should be proper facilities for meat inspection. Many of the slaughterhouses in this country have for long been justifiably criticised, both because of the inhumane conditions under which many of the animals were slaughtered and on public-health grounds. Moreover, slaughterhouses, especially in rural districts, are so numerous that it is well-nigh impossible for local authorities to ensure that the carcases and organs of all animals slaughtered for human food are satisfactorily inspected before being offered for sale.

In the late war the taking over of slaughtering and marketing of livestock by the Ministry of Food brought about a reduction in the number of slaughterhouses in England and Wales from some 12,000 to about 500, and it was expected that the Government would seize the opportunity to forbid any reversion to slaughter on private premises, in accordance with a policy of moderate concentration.

Before the war enlightened opinion had accepted the desirability of such a policy, and an inter-departmental committee was set up to state general principles of siting slaughterhouses under this policy. Instead, since control by the Ministry of Food was brought to an end, licensed slaughterhouses in England and Wales have reached a total of some 4500; and the Slaughterhouses Bill, which has lately had its second reading in the House of Commons, provides that, subject to a certain limit of time, a private trader is free to build a new slaughterhouse or modernise his existing premises. What advantage the private trader will take of this facility is uncertain; but clearly the policy of moderate concentration has been discarded. Public-health authorities will regard this retrogressive step with consternation; for it may once again become impossible to inspect all meat to be consumed. Already

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4. Pellew, R. A. A. *Med. J. Aust.* 1951, i, 944.
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10. Wiles, P., Andrews, P. S., Devas, M. B. *ibid.* 1956, **38B**, 95.
11. Smillie, I. S. Injuries of the Knee Joint. Edinburgh, 1950.
12. Somerville, E. W. *J. Bone Jt Surg.* 1946, **28**, 451.

many local authorities are experiencing difficulty in maintaining a properly qualified staff of inspectors, because of poor salaries and the unpleasant and at times dangerous nature of the work.

This sombre picture is relieved by only one ray of light—draft regulations have been published setting out minimum standards for the layout and equipment of slaughterhouses in England and Wales, with the purpose of securing humane slaughter and hygienic conditions. How much better it would have been if moderate concentration of slaughterhouses had been sought at the same time.

PANCREATIC CHANGES PRODUCED BY CORTISONE

IN view of the profound influence which cortisone and allied substances exert on the metabolism of carbohydrates—culminating in "steroid diabetes"—it is not surprising that early studies of the effects of these hormones on the pancreas were concerned with changes in the islets of Langerhans.[1 2] But the pancreatic acinar tissue also undergoes pathological modifications. Prompted by experimental studies on the pancreatic changes in rabbits treated with cortisone,[3–5] Carone and Liebow [6] have examined sections of the pancreas taken at necropsy from 54 patients who had been treated with cortisone, prednisone, prednisolone or corticotrophin, and found histological evidence of acute pancreatitis or fat-necrosis in 16 cases. Of a control series of 54 similar but untreated cases, 2 showed evidence of acnte pancreatitis but no fat-necrosis. Microscopically, the patchy lesions observed were not extensive; in only 3 cases were they "severe." The pancreatitis was mainly interstitial, and necrosis of the acinar cells and hæmorrhage were not prominent. The mildness of these changes contrasts with those described by Baar and Wolff [7] in their 2 cases of hæmorrhagic pancreatic necrosis in children treated with cortisone.

An additional pathological change—ectasia of the pancreatic acini—was observed by Carone and Liebow [6] in 32 of their 54 cases. This resembled the changes evoked by administration of cortisone in rabbits. The acini were dilated, their lining cells were flat and devoid of granules, and the lumen of the ectatic acini—which now looked like ductules—contained presumably inspissated secretory material. Similar changes have been described in various diseases, and were indeed, present in 13 of Carone and Liebow's 54 untreated control cases; but the fact that such changes can be produced experimentally by the administration of cortisone or corticotrophin alone suggests that adrenocortical secretion may possibly contribute to these changes, even where no cortisone has been administered.

The nature of these changes is far from clear. Since it has been suggested that treatment with corticotrophin or cortisone can produce a state not unlike chronic inanition,[8 9] the acinar changes produced by adrenocortical steroids might be the indirect result of the metabolic disturbance caused by these hormones, but convincing evidence of this is lacking. A relation to the changes in the islets of Langerhans and to the deranged metabolism of carbohydrates can be ruled out.[4 5] Stumpf et al.[4] noted in rabbits treated with cortisone a fairly close relation between the incidence and severity of acinar lesions on the one hand and increase in the blood-level of neutral lipids on the other; severe pancreatic lesions, with a raised blood-amylase level, were present most commonly when cortisone produced "an unusually sharp rise" in the blood-level of neutral fats without a simultaneous increase of the levels of cholesterol or phospholipids. Since the hyperlipæmia appeared before the pancreatic lesions, Stumpf et al. suspected that the increase in blood-lipids induced by cortisone might be a factor in the pancreatic damage. Benscombe and Lazarus,[5] on the other hand, found some similarity between the lesions produced by cortisone and those found after ligation of the pancreatic duct, and concluded that cortisone produced possibly intermittent but progressive obstruction of the pancreatic intralobular ducts either by stimulating directly the duct epithelium or by altering the viscosity of the pancreatic secretion. Carone and Liebow [6] and Baar and Wolff [7] advanced a similar explanation of the changes in their necropsy cases.

These observations suggest several questions of interest to the clinician. Can the pancreatic lesions be diagnosed during the life of the patient? In Carone and Liebow's [6] series these changes had not been suspected; no symptoms or signs pointing to the pancreas had been recorded; but these workers realise that such manifestations might not have been noticed because of their mildness, or the administration of the cortisone might have masked them. Stumpf et al.[4] reported a definite increase in the blood-amylase level in 34 of 36 rabbits treated with cortisone. It would clearly be useful if this change and perhaps hyperlipæmia could be detected in patients treated with cortisone. In the series of Carone and Liebow [6] there was no evident relation between the duration and the intensity of the steroid treatment given and the incidence of the lesions. The diversity in response between different individuals should be borne in mind when contrasting the reported favourable results in severe acute pancreatitis treated with cortisone [10–12] with the rather severe pancreatitis apparently caused on occasion by cortisone.[7]

DYE-DILUTION TESTS IN CONGENITAL HEART-DISEASE

THE surgical correction of congenital cardiac defects is one of the notable achievements of the present decade. Often the site and nature of a defect can be confidently predicted from the clinical evidence alone; but sometimes this, together with special radiographic studies and measurements of pressure and oxygen content at cardiac catheterisation, does not enable an accurate diagnosis to be made. A further test, largely developed at the Mayo Clinic, is therefore of considerable interest.

The method depends on photometric recording, at a point distal to the lesion, of a dye substance introduced into the circulation proximal to the lesion. In the healthy person an injection of a suitable indicator into the right atrium will be recorded at the radial artery by an almost symmetrical deflection, the appearance-time of which is about 10 seconds; a second curve of much diminished amplitude, with its peak from 12 to 18 seconds after the peak of the initial deflection, represents the average time taken by the blood to recirculate. Abnormal circulatory pathways result in typical alterations of this pattern, which can be demonstrated by suitable selection of the injection and sampling sites.

The radial artery is a convenient sampling site, and blood is withdrawn at a constant rate by means of an indwelling needle connected to a length of polyethylene tubing which traverses a cuvette oximeter.[13] Skin photometers, such as those designed for attachment to the

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ear pinna, have also been used, but are less sensitive and may fail to detect the smaller changes in infants and children.[14] Evans-blue (T-1824), the dye used in most studies, has the disadvantage that its spectral absorption coincides with that of reduced hæmoglobin. Hence, its use in cyanosed patients is limited since the oximeter cannot distinguish between it and reduced hæmoglobin. The introduction of a new dye—tricarbocyanine dye II—which can be detected independently of the blood-oxygen saturation widens the scope of this form of investigation to include left-to-right shunts, continuous recording of cardiac output, and blood-flow measurements in limbs and organs.[15]

This method is readily applied in the diagnosis of central shunts. In the presence of a right-to-left shunt injection of dye into the superior vena cava will result in a characteristic abnormal curve in which the appearance-time of the initial deflection is much shortened owing to bypass of the pulmonary circuit by some of the dye (the so-called double-humped curve). The demonstration of such a curve in patients with tight pulmonary stenosis complicated by a septal defect may be particularly helpful; after injections of dye into the right atrium and right ventricle, abnormal curves in both instances indicate a ventricular septal defect, whereas if only the former curve is abnormal the shunt is interatrial.[16]

Left-to-right shunts also produce typical changes: the amplitude of the initial deflection is reduced, owing to excessive dilution of the dye by the shunting blood, and the disappearance-slope is prolonged, owing to the increase in recirculation which may produce a small hump. Such curves are useful in differentiating between a high ventricular septal defect, aortopulmonary defect, and patent ductus arteriosus when the oxygen saturation of blood-samples at cardiac catheterisation are all similar owing to the proximity of the suspected sites. In such cases, using retrograde catheterisation of an artery, the dye is injected at the root of the aorta and again near the origin of the left subclavian artery. Normal curves at both sites show the shunt to be proximal to the aortic valve; abnormal curves at both sites indicate patent ductus arteriosus; an abnormal curve following injection at the root of the aorta with a normal or near-normal curve following injection near the origin of the left subclavian artery indicates an aortopulmonary defect.[16] Such information helps the surgeon to prepare for an intra- or extra-cardiac operation.

Occasionally it proves difficult to advance the tip of the cardiac catheter beyond the pulmonary or tricuspid valve, and it may be important to determine whether atresia is in fact present. If this is so, there can only be one circulatory pathway, reflected by essentially similar curves from the proximal chambers and the left atrium, which can usually be readily entered in these cases. Conversely, patency of the pulmonary or tricuspid valves results in obviously dissimilar curves following injections of dye into the two fitria.[17] Another occasional difficulty at catheterisation is in identifying anomalous vessels, since complex malformations are commonly accompanied by transposition. The injection of dye then provides information as to whether the catheter tip is in the aorta or pulmonary artery.[18] The technique of indicator-dilution can also be applied to the diagnosis of peripheral arteriovenous fistulæ,[14] anomalous pulmonary venous drainage,[19] and valvular regurgitation.[20 21]

As Wood et al. rightly point out, this form of investigation is valuable in truly reflecting the hæmodynamic state. The technique is so relatively simple that it is likely to become a routine part of cardiac catheterisation.

NEW HOSPITALS

IN this country ten years after the war we are still making do with our old hospitals. We do not grudge new hospitals to the underdeveloped countries or to the war-damaged countries. We can only admire the enterprise and good will of the citizens of expanding countries who have found the money to build more hospitals. But those who work in the hospitals of Britain would be less than human if they did not sometimes resent our growing eligibility for the title of the "only country which has not built a post-war hospital". Extant, more or less weather-proof, yearly growing more obsolescent, inefficient, at times verging dangerously on the unhygienic, our hospitals continue to stand, and by their existence allow our inactivity to continue. But as Mr. J. F. Milne points out in his editorial foreword to the *Hospitals Year Book* for 1958 [1], not only are we steadily falling behind other countries in the standard of our hospitals, but we are piling up building arrears which will sooner or later have to be made good.

Many of our hospitals when they were built were the best that money and skill could provide. Others were monuments to British resource, often in difficult times of war. These, not unnaturally, have withstood less successfully the combined tests of time and ever-growing demands. Some years ago Miss Elaine Burton [2] described a hospital in which the ophthalmic unit was a chicken-farm unit bought in Norfolk and erected by the hospital staff, the children's ward of air-raid shelter construction, and the tonsil unit originally built as a gas-decontamination unit. No doubt few hospitals are, or ever were, such triumphs of improvisation over matter, but too many are less than satisfactory. It is never wise to confuse parsimony with thrift, and already out-of-date cooking and heating equipment is costing us dear in maintenance while inadequate ventilation and sterilisation plants have proved a hazard in the operating-theatre.[3]

To say that standards in some places are still too low is not to belittle the improvements that have been achieved, sometimes in those very places and often with very little money eked out by hard work and hard thinking. But this is trembling once more on the brink of improvisation, and in the long run nothing can take the place of an occasional brand-new building. Since the war we have rightly found the money to build some much-needed new schools. The Ministry of Health's approval of a building programme of over £17 million for 1956-58 showed belated official recognition that the hospitals' turn could not with safety be postponed much longer, and this has been confirmed by the Chancellor's exemption of hospital building from his recent cuts in public capital expenditure. But at the present value of money the Minister's proposed allocation (announced on p. 1234) of £22 million for capital development in 1959-60, no more than holds the current level of £20 million, and still lags far behind the £30 million proposed by the Guillebaud Committee. It is good news that projects for three new hospitals have reached their second phase; at Swansea and Swindon plans have already begun to change into bricks and mortar and at Huddersfield site work is in hand. These real if overmodest beginnings should not, however, lead us to neglect Mr. Milne's warning that if our hospital services are to be adequately maintained double or treble the present amount must be found each year for capital development.

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1. Obtainable from the Institute of Hospital Administrators, 75, Portland Place, London, W.1. Pp. 1112. £2 15*s*.
2. See *Lancet*, 1953, ii, 1362.
3. *ibid.* 1956, ii, 1197.

Special Articles

THE OSMOTIC BEHAVIOUR OF THE BODY CELLS IN MAN*

SIGNIFICANCE OF CHANGES OF PLASMA-ELECTROLYTE LEVELS IN BODY-FLUID DISORDERS

VICTOR WYNN
M.D. Melb.
SENIOR LECTURER IN SURGERY, ST. MARY'S HOSPITAL MEDICAL SCHOOL, LONDON

THE factors which control the hydration of mammalian tissues are not yet completely known. Unlike easily separable cells—such as erythrocytes and the egg cells of certain marine invertebrates—the tissue cells cannot be subjected to the precise measurement of pressure-volume relationships in response to osmotic changes. Nor is it safe to argue from erythrocytes, &c., to the behaviour of tissues. The possible influence of disease on the osmotic behaviour of tissue cells makes such assumptions even more uncertain.

The subject is of theoretical and practical importance. Osmotic stresses, by which is meant a change in the relationship of water to the total number of solute molecules and ions, develop commonly in many illnesses. It would simplify the diagnosis and treatment of such disorders of the body fluid if it could be shown that the osmotic behaviour of the body cells, taken as a whole, was predictable. Any significant departure from predicted behaviour in a given case would then be a notable feature worthy of further study, possibly leading to new knowledge of the underlying pathological process. But until the usual response of body cells to osmotic stresses is known, the numerous clinical and experimental reports of unusual osmotic mechanisms observed under special conditions cannot be assessed.

The account given here of the osmotic behaviour of the body cells as a whole is based on clinical observations and experimental studies in man. As in all such studies, the approach is indirect and involves certain assumptions and approximations. Nevertheless, the results support the view that, in osmotic stresses in health and disease, the body cells behave as predictable osmotic systems. The practical application of these results to the management of body-fluid disorders will be discussed.

Osmotic Theory applied to Body Cells

If cells were ideal osmotic systems—i.e., ideal dilute solutions encased in a semipermeable membrance offering no resistance to change of volume—osmotic adjustments would take place by the movement of water across the cell membrane until the osmotic pressure was the same on the two sides of the membrane. Such a cell could be described as a perfect osmometer (Ponder 1940). Its hydration would depend passively on the content of osmotically active† solutes in the cell and on the concentration of such solutes in its environment (the extracellular fluid). The actual organisation of the cell, however, is more complex than this static view allows.

Cell membranes are not impermeable to the major solutes of the body fluids (the inorganic electrolytes). Most cells (the erythrocytes of certain animals are exceptions) actively maintain ionic gradients whereby the sodium which enters the cells is mostly extruded, whereas the potassium is retained.

The mechanism for this is not completely understood. Two possibilities are suggested: (1) the extrusion of sodium is an active process depending on the metabolic energy of the cell (Ussing 1954, Conway 1957); and (2) there is selective intracellular accumulation of potassium (Ling 1955).

As regards the present argument, it is immaterial how ionic gradients are maintained. So long as the mechanism is intact and restraint is placed on the distribution of the solutes, the cell membrane may be regarded as if it were semipermeable, and the movement of water would still be determined passively by the concentration of solutes.

Many experimental and clinical observations, however, seem to conflict with this "simple osmometer" theory of cell behaviour (Robinson 1953, Opie 1955, Brodsky et al. 1956). Other explanations have been put forward:

(1) Robinson (1950) pointed out that osmotic equality between cells and extracellular fluid has been widely assumed but never conclusively proved. He postulated a higher intracellular than extracellular osmolarity, depending on an energy-consuming process which pumps water out of the cell against an osmotic gradient. The water balance of the cell would not then depend passively on extracellular changes unless the osmotic gradient was constant. Robinson's conclusions may apply to certain specialised cells—e.g., renal tubules and liver—but are unlikely to apply to the main mass of tissue cells (Conway and McCormack 1953, Leaf 1956).

(2) The osmotic activity of cell solutes may be altered (either decreased or increased) independently of the nett movement of water or of solutes into or out of the cell. First put forward by Elkinton et al. (1944) and clearly restated by Elkinton and Danowski (1955), this hypothesis assumes that the osmotic activity of cell cations may be altered without change of total concentration (e.g., by complexing reactions akin to those seen with chelating agents), or that a similar osmotic effect may be produced by changes in the size and degree of dissociation of molecular aggregates, such as proteins and organic phosphates, within the cell.

(3) Osmotic adjustments may take place by the movement of solutes into or out of the cells, water being transferred secondarily as a consequence of these shifts of solutes. Such movements have been described by Elkinton and Taffel (1942) during water-depletion experiments on dogs and may be inferred from the results of Black and Milne (1952) on depletion of potassium in man.

(4) Under certain conditions cell hydration may depend on factors other than extracellular osmolarity. For example, when cell respiration is inhibited by drugs or by cooling, the cells swell with fluid (Stern et al. 1949), the imbibed fluid having essentially the same composition as extracellular fluid with certain modifications predictable on theoretical grounds (Leaf 1956). A clinical counterpart to this phenomenon may be the observation by Hills et al. (1953) of increased cell hydration in states of adrenocortical insufficiency, and its reversal by the administration of cortisone but the observations need confirmation. How cell hydration is affected by disturbances in the energy level of the cell remains to be explored in clinical conditions. Deficiencies in cellular metabolic energy have been invoked to explain some of the disorders seen in patients (Moore et al. 1956, Elkinton 1956).

Experimental Approach to Study of Osmotic Adjustment of Cells in vivo

Osmotic stresses in man involve a change in the total amount of body water or of osmotically active solutes, or of both. These changes can be measured, but their effect on the body cells cannot be studied directly. To find out how nearly ideal in their osmotic properties are the cells as a whole, an indirect method involving a study of the extracellular fluid can be used. As suggested by Elkinton et al. (1944), an osmotic formula relating change in extracellular osmolarity to change in the balance of water and solutes can be derived as follows:

If we assume that cells behave as ideal osmotic systems, then at equilibrium the concentration of osmotically active solutes (mM per litre) is the same throughout the whole of the body water—i.e., the extracellular osmolarity (E.O.P.) equals the intracellular osmolarity (I.O.P.). (More correctly, I.O.P. would be greater than E.O.P. by the small pressure exerted

* The substance of this paper was given as a lecture at the Postgraduate Medical School of London, on Nov. 21, 1956.

† Solutes such as urea, to which the cell membrane is freely permeable, and which are distributed equally throughout body water, are not held to be osmotically-active in the present context.

by the membrane tension, but for the present purposes this small difference can be ignored.)

Let E.O.P.$_1$, E.O.P.$_2$ = initial and final osmolarities (mM per litre) of the extracellular fluid.

W_1, W_2 = initial and final total amounts of body water (litres).

A_1, A_2 = initial and final total amounts of osmotically active solutes in body water (m. moles).

ΔA = change in such solutes.

then, at equilibrium,

A_1 = (E.O.P.$_1$ × W_1)

After a change in total body water from W_1 to W_2, and a change (ΔA) of total osmotically active solutes,

then, at equilibrium,

A_2 = (E.O.P.$_2$ × W_2) = $A_1 + \Delta A$

but $A_1 + \Delta A$ = (E.O.P.$_1$ × W_1) + ΔA

$\therefore$ (E.O.P.$_1$ × W_1) + ΔA = (E.O.P.$_2$ × W_2)

This general form of the osmotic formula can be modified to make it more readily applicable to clinical problems, without much loss of accuracy, in the following way :

In the absence of hyperglycæmia the effective extracellular osmolarity is almost entirely due to the total ionic concentration—i.e., the sum of the cations sodium, potassium, calcium, and magnesium and their accompanying anions. Since mostly univalent ions are involved, the total cations and anions are nearly equal ; hence if [B] represents the total extracellular cation concentration, a close approximation to the effective osmolarity of extracellular fluid is given by 2[B]. (For simplicity the incomplete dissociation of the electrolytes is ignored because it affects both sides of the equation equally.)

The change in total osmotically active solutes (ΔA) may be measured approximately by the external balances of sodium and potassium and their accompanying (mostly univalent) anions. The balances of calcium and magnesium are small in acute osmotic stresses and can be ignored. ΔA can now be represented as 2bB, where bB is the algebraic sum of the external sodium and potassium balances. This approximate value for ΔA would be affected if there were hyperglycæmia (because ΔA would increase without being reflected in the external electrolyte balance) ; if the urine were alkaline and the excretion of phosphate large (because the base equivalence of PO_4^{--} would be greater than 1, and hence the excretion of anions would be less than excretion of cations) ; and if there was a large transfer of H^+ into or out of the cells (see Swan and Pitts 1955). In the present experiments care was taken to minimise, as far as possible, these factors affecting the approximations used in the osmotic formula.

The osmotic formula may now be rewritten as follows :

$$2[B_1] \times W_1 + 2bB = 2[B_2] \times W_2$$

and finally

$$[B_1]W_1 + bB = [B_2]W_2.$$

Use of the Osmotic Formula

The measurements needed to apply the osmotic formula can readily be made. If, under a variety of osmotic stresses and many different clinical conditions, it can be shown that the observed extracellular osmolarity agrees with the predicted, this would be strong evidence in favour of the hypothesis on which the osmotic formula is based. The concept of osmotic activation and inactivation would be seriously weakened, as would the existence of intracellular hypertonicity, at any rate as applied to the mass of body cells. The osmotic formula described here would not distinguish between adjustments based on shifts of water alone and those due to shifts of electrolytes alone, but other measurements can be combined with the study of extracellular osmolarity which bear on this aspect (see below).

Methods

All the experiments were similar in plan and consisted in estimating the plasma-electrolyte levels and the total amounts of body water before and after a measured change of water and electrolyte balance produced over a period of about twenty-four hours. In some patients repeated observations were made on up to five consecutive days, each twenty-four-hour period being regarded as a separate experiment.

The Patients

10 patients (cases 1–10, 34 experimental periods) were studied for up to five days postoperatively, and 3 patients (cases 11–13, 15 experimental periods) for five days soon after the onset of a severe non-surgical trauma (coronary occlusion in 2 cases, and dissecting aortic aneurysm in 1).

The 49 balance periods in this group of 13 subjects served to define osmotic behaviour in a varied group of illnesses, and in the presence of acute trauma. Full metabolic details of these cases are given elsewhere (Wynn and Houghton 1957).

13 other patients (cases 14–26, 31 experimental periods) had various disturbances of water and electrolytes (table I).

Metabolic Methods

The patients were studied in a metabolic ward. External electrolyte and nitrogen balances were measured in the usual way as the difference between intake and output. The intake was very largely, or entirely, by intravenous infusion, which was virtually stopped for at least two hours before blood was taken for analysis, so as to allow time for osmotic equilibrium to be achieved. Water balance was calculated from the formula of Lavietes (1935).

Body-weight changes were measured in bed-patients by using special scales (Avery type 33N) which weighed the whole bed. The scales were sensitive to 30 g. and were checked by certified weights. Ambulant patients were weighed on personal weighing scales sensitive to 15 g. (Avery type 3302 ABN).

Chemical Methods and Calculations

The chemical methods are described elsewhere (Wynn and Houghton 1957). Total body water was measured once in each patient by the antipyrine method (Soberman et al. 1949), except in 3 patients in whom a tritium method ‡ was used. Total body water was usually measured at the end of the study, and, in patients studied for more than one twenty-four-hour period, the daily water-balance figure was used to calculate the total body water relevant to each experimental period.

The method of calculating the total cation content of extracellular fluid [B] was as follows :

The extracellular sodium level [Na_e] = plasma [Na]$x\gamma$ where γ is a factor correcting for plasma-water and the Donnan effect, and equals

$$\frac{0.344}{\text{Plasma-water}} + 0.671 \text{ (Leaf et al. 1954).}$$

To [Na_e] is added the observed value of the plasma-K level plus 3·5, the latter figure being taken to represent the amount of Ca and Mg. in the extracellular fluid and assumed not to vary during the period of observation.

Since hyperglycæmia introduces into the calculations a complication which cannot with certainty be corrected, care was taken to prevent it, and if the plasma-glucose varied by more than 50 mg. per 100 ml. (2·7 mM per litre) from the initial value the period concerned was excluded from consideration.

Results

The metabolic data for cases 14–26 are set out in table I, and the data for cases 1–13 are recorded elsewhere (Wynn and Houghton 1957).

The changes (Δ [B]) in the total cation level of the extracellular fluid for all the cases are shown in the accompanying figure, the values predicted by the osmotic formula being plotted as ordinates and the observed values as abscissæ. It will be seen that the present cases predominate among the group with the greatest osmotic stress—i.e., the greatest change in [B].

The correlation between predicted and observed Δ [B] is clear from the graph : the regression equations are

‡ I am indebted to Dr. I. MacIntyre, of the Postgraduate Medical School, Hammersmith, for these estimations.

TABLE I—METABOLIC DETAILS AND DIAGNOSIS IN CASES 14—26

Case no.	Water balance (ml.)	External balance (mM)				Initial total body water (litres)	Initial [B] (mMper litre)	Δ[B]P* (mM per litre)	Δ[B]o* (mM per litre)	Δ[B]P−Δ[B]o (mM per litre)	Diagnosis
		Na	K	Cl	HCO_3						
14	+5330	+336	− 10	+724	—	31·4	168·2	−15·5	−15·3	+0·2	Pyloric obstruction with predominant water depletion corrected with salt and water infusion
15	+ 520	+390	− 17	+372	—	29·9	127·1	+10·1	+10·6	−0·5	Chronic postoperative water retention treated by hypertonic saline solution
16	+ 825	− 25	− 12	− 32	—	9·9	145·3	−14·6	−16·7	−2·1	Postoperative hypotonicity
17	+3050	−272	− 15	−263	—	43·0	149·2	−16·0	−16·5	−0·5	Healthy subject, experimental water intoxication, and its correction
	−3700	+ 29	− 4	+ 53	—	46·0	133·0	+12·4	+14·0	−1·6	
18	+ 125	+648	− 54	+623	—	41·9	150·8	+13·8	+15·4	−1·6	Healthy subject, experimental hypertonicity, and its correction
	+5000	− 51	− 50	− 63	—	42·0	166·2	−19·8	−21·1	−1·3	
19	+6800	− 27	− 33	− 30	—	42·8	168·3	−24·4	−27·4	−3·0	Diabetes insipidus; hypertonicity corrected by water infusion
20	−2315	+113	− 31	+107	—	35·6	155·3	+13·6	+12·3	+1·3	Diabetes insipidus with experimental hypertonicity due to water depletion
21	−200	+494	+ 27	+ 73	—	33·8	146·8	+16·3	+15·7	+0·6	Sodium depletion and uræmia treated by hypertonic $NaHCO_3$ infusion
22	± 0	+678	− 41	+281	+445	31·1	138·5	+20·5	+21·3	−0·8	Sodium depletion and uræmia treated by hypertonic $NaHCO_3$ infusion
23	± 0	+414	− 18	+397	—	26·4	123·6	+15·1	+14·6	+0·5	Respiratory failure, water intoxication treated by hypertonic saline infusion
	− 400	+666	− 48	+618	—	26·4	123·6	+25·8	+25·6	+0·2	
24	−5060	−610	−209	−332	−442	46·8	145·1	− 2·0	− 4·1	−2·1	Cardiac failure, cor pulmonale, treated by diuretics
25	−3200	−470	− 81	−224	−320	30·4	152·3	− 2·3	− 2·1	+0·2	Cardiac failure, cor pulmonale, treated by diuretics
26	−6200	−593	−195	−810	—	34·8	147·2	+ 4·3	+ 3·3	+1·0	Cardiac failure, treated by diuretics

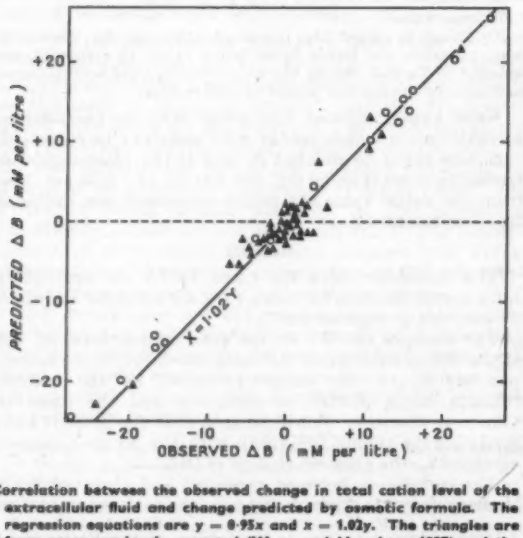
*Δ[B]P Δ[B]O predicted and observed change in [B] respectively.
Initial [B] = E.C.F. total cation level calculated as described in the text.
Metabolic details of cases 1–13 are given elsewhere (Wynn and Houghton 1957).

$y=0{\cdot}95x$, and $x=1{\cdot}02y$. It follows that the osmotic formula predicts with reasonable accuracy the change in the total cation level of the extracellular fluid, at least over the range of ± 26 mM per litre.

The figure shows that the observations can be divided into three groups: (1) 46 observations in which the change in osmolarity was less than ± 8 mM per litre, and mostly less than ± 3 mM per litre; (2) 7 observations in which the change was a large decrease of osmolarity (greater than −15 mM per litre); and (3) 12 observations in which there was a large increase in osmolarity (greater than +15 mM per litre.

The accuracy of prediction in these three groups is compared in table II. The mean differences between predicted and observed [B] do not differ significantly from zero, or from each other, and the standard deviation (σ) is similar in the three groups.

The osmotic formula therefore applies equally whether the osmotic stress is small or large, and whether the change is an increase or a decrease in osmolarity. Two-thirds of the predictions are within 1·6 mM per litre of the observed total cation level of the extracellular fluid. This agreement is good in view of the approximations involved in the calculations and the effects of possible analytical and other errors on the results.



Correlation between the observed change in total cation level of the extracellular fluid and change predicted by osmotic formula. The regression equations are $y = 0{\cdot}95x$ and $x = 1{\cdot}02y$. The triangles are from cases previously reported (Wynn and Houghton 1957) and the circles from present cases.

Osmotic Behaviour in Congestive Cardiac Failure (cases 24, 25, and 26, table I)

Since cardiac failure provides so many of the clinical examples of osmotic disturbances, especially of hypotonicity, and since there are many reports of unusual osmotic responses in this condition, the present group is of special interest. Cases 24 and 25 had respiratory insufficiency as well as heart-failure, and in both cases the diuresis involved a large loss of bicarbonate in the urine, thus presenting an unusual osmotic stress. Case 26 showed in his urine the typical electrolyte pattern of a mersalyl diuresis potentiated by ammonium chloride. In these 3 cases the osmotic response was indistinguishable from normal. In cases 24 and 26 the large loss of potassium was a notable feature. The osmotic formula assigns the same osmotic value to potassium as to sodium, an assumption supported by evidence presented elsewhere (Wynn and Houghton 1957). Cases 24 and 26 provide further support for this thesis.

Osmotic Behaviour in Chronic Hypotonicity

Cases 15 and 23, with chronic water intoxication, are of interest as the only cases, in the present series, of severe hypotonicity treated with hypertonic saline infusions. The osmotic response was normal.

Osmotic Behaviour in Chronic Acidosis and Sodium Depletion

The osmotic prediction formula is based upon the idea of a uniform osmolarity throughout body water and the absence of sites of significant activation or inactivation, or segration or release of osmotically active solutes. Recently attention has been directed to the skeleton as an electrolyte reservoir, since there are large amounts of sodium in bone not in solution in water but forming an integral part of the bone crystals (Bergstrom 1956, Nichols and Nichols 1956). The metabolic function of this bone sodium has not yet been fully elucidated, but the suggestion has been made that it may be released in certain circumstances which mostly involve depletion of sodium and chronic acidosis. The amount of sodium so released may amount

to 200–300 mM in an adult weighing 70 kg. (Nichols and Nichols 1956).

In cases 21 and 22 sodium depletion and acidosis existed for several days, at least, before treatment. The plasma biochemistry before and after treatment is given in table III. Treatment with hypertonic infusions of sodium bicarbonate produced osmotic changes as predictable as in the general group of cases (table I). Hence there was no evidence in these two cases that sodium had re-entered bone in sufficient amounts to disturb the accuracy of osmotic prediction, at any rate over the period (twenty-four hours) of the present study. The results are in agreement with the views of Bergstrom (1956), who showed, in rats, that sodium was not taken up by sodium-depleted bone for up to five days after sodium infusion had corrected the deficit of extracellular sodium and the acidosis. Therefore the data reported here do not support the suggestion of Nichols and Nichols (1956) that the electrolyte reservoir in bone may explain the discrepancies reported in balance studies of osmolarity changes.

Shifts of Electrolytes in Osmotic Stresses in Man

If electrolytes move across the cell membrane in response to osmotic stresses, it is reasonable to look first for such movements as might protect the cell against changes in osmolarity of the extracellular fluid. In hypotonic stresses increase in cell volume would be reduced if intracellular solutes were released, the most likely being

TABLE II—ACCURACY OF PREDICTION OF Δ [B] IN GROUPS 1, 2, AND 3

Group		1	2	3
No of observations	..	46	7	12
Mean of $\Delta[B]_P$* (mM per litre)	..	1·9†	—19·4	+15·2
$\Delta[B]_P - \Delta[B]_O$ (mM per litre)	mean	−0·10	−1·0	−0·2
	S.D.	1·58	1·41	1·15
Significance of	t	0·43	1·88	0·53
Difference from zero	P	0·6<P<0·7	0·1<P<0·2	0·6<P<0·7

Group 1 represents the cases with minimal changes in osmolarity.
Group 2 represents the 7 cases with maximum hypo-osmolarity (see fig. 1).
Group 3 represent the 12 cases with maximum hyper-osmolarity (see fig. 1).
*$\Delta[B]_P$, $\Delta[B]_O$ = predicted and observed change in [B] respectively.
† Sign is disregarded in calculating this mean.

potassium as being in greatest supply. Conversely, in hypertonic stresses the reverse might be expected—i.e., conservation of potassium.

In the present three groups the mean twenty-four-hour potassium balance was negative, but there was no significant difference between the three groups (table IV).

In groups 1 and 3 there was no significant change in the plasma-K level, whereas in group 2 the plasma-K fell, on the average, by 0·6 mM per litre (table IV). This fall was presumably largely due to dilution of the extracellular fluid and was in the reverse direction from what would be expected if the change protected the cell against the osmotic effects of such dilution.

Acute osmotic stresses therefore seem to be without noticeable effect on cell potassium other than what might be expected as a consequence of disease or trauma, which was the background against which most of the observations were made. These observations apply only to acute experiments over twenty-four hours and do not exclude the possibility of significant shifts of potassium in response to more prolonged osmotic stresses.

Whether or not there are significant movements of sodium (and accompanying anions) into or out of the cells in response to osmotic stresses cannot be answered from the present data. Calculations based upon changes in the chloride space, so popular in the past literature, are now thought to be invalid (Conway 1957) and have not been attempted here. The nature of the clinical material precluded the possibility of direct measurement of the volume of the extracellular fluid by infusion techniques; so this crucial question still awaits answer.

TABLE III—PLASMA BIOCHEMISTRY BEFORE AND AFTER TREATMENT IN CASES 21 AND 22

Case no.	Na (mM per litre)	K (mM per litre)	Cl (mM per litre)	HCO_3 (mM per litre)	pH	Non-protein nitrogen (mg. per 100 ml.)
21 ..	134·5	3·35	108	12·4	7·28	90
	150·0	3·2	109	27·3	7·42	78
22 ..	125·0	5·0	99·0	13·6	7·31	68
	147·0	3·5	104·0	26·6	7·42	60

Discussion of Results

The results reported here support the view that the tissue cells as a whole behave in vivo as perfect osmometers. They amplify similar observations in man (Wynn and Houghton 1957) and extend to the clinical field experiments in animals which have led to the same conclusion (Leaf et al. 1954, Wolf and McDowell § 1954, Wynn 1955). Against this hypothesis, however, can be listed a rather formidable array of papers which, besides those already mentioned, include: Wilson et al. (1954), Dudley et al. (1954), Wilson (1955), De Cosse et al. (1956), Graber et al. (1956), and Zimmerman et al. (1956) dealing specifically with the problem of postoperative hypotonicity; Iseri et al. (1950), Squires et al. (1951), Mader et al. (1955), and Iseri et al. (1955), dealing with electrolyte metabolism in congestive cardiac failure; Dieckmann and Pottinger (1955) with reference to eclampsia; Flanagan et al. (1950); Hills et al. (1953); Robertson and Dunihue (1954) and Cheek and West (1956) dealing with effects of adrenocortical hormone on tissue hydration; and Woodbury (1956) reporting the effects of acute sodium depletion on tissue hydration (in rats). Woodbury concludes that each tissue has its own intrinsic control of the metabolism of electrolytes and water. This idea appeals generally to physiologists because it endows the cells with mechanisms which would protect them against the osmotic effects of changes in osmolarity of the extracellular fluid and would therefore have considerable survival value.

I cannot here review these conflicting observations. But it should be said that the value of several reports is reduced because some measurements necessary for the calculations were not made, but assumed values were used—e.g., for total body water and water balance. Sometimes potassium balance was not measured or was ignored; in only one report (Leaf et al. 1954) was the effect of hyperglycæmia considered. Of particularly doubtful validity are conclusions based upon the use of the "chloride space" as a measure of change of volume of the extracellular fluid (Conway 1957).

The "perfect osmometer" hypothesis presented here has the merit of simplicity but must at present be

TABLE IV—CHANGES IN PLASMA-K AND 24-HOUR EXTERNAL K BALANCE IN GROUPS 1, 2, AND 3

Group	1	2	3
No. of observations ..	46	7	12
Mean Δ plasma-K (mM per litre)	− 0·07	− 0·61	+0·10
Mean 24-hr. K balance (m.moles)	−25·0	−44·9	−32·5
S.D.	30·4	37·5	26·2
Significance of difference from group 1	t	1·51	0·78
	P	0·1<P<0·2	0·4<P<0·5

§ Later and more searching experiments led these authors to modify somewhat their former views (McDowell et al. 1955), but the main conclusions about the agreement between predicted and observed Δ [B] remain unaffected.

regarded as only an approximate description of events as they actually occur in tissues. A satisfactory quantitative formulation of the problem must await the development of suitable techniques for the precise measurement of the functional volume of the extracellular fluid, and more knowledge about the distribution of ions and of ionic activities in the tissues.

Whatever the final solution of the problem of the osmotic behaviour of the tissue cells proves to be, the present results may be used to resolve certain clinical questions important to clinician and clinical biochemist. They show that, in a wide variety of clinical conditions (and perhaps all) acute changes in the body's content of water and electrolytes (sodium, potassium, and their accompanying anions) will have predictable effects on the total ionic concentration of the extracellular fluid. Conversely, changes in the effective osmolarity of the extracellular fluid are quantitatively related to changes in the body's water and electrolyte balance. (The modifying effect of hyperglycæmia on this concept, previously mentioned, must be borne in mind and will not be further considered here.)

The pathogenesis of certain body-fluid disorders becomes clearer in the light of this thesis. For example, plasma hypotonicity (low plasma-[Na] level) is almost invariable after surgical operations, although sodium may be retained in the body (Moore and Ball 1952). The cause of this metabolic disorder, a controversial subject, has been shown to be retention of water and loss of potassium (Wynn and Houghton 1957). A similar pathogenesis applies to several other conditions with manifest hypotonicity—e.g., congestive cardiac failure (Laragh 1954), hepatic failure with ascites (Talso et al. 1956), and progressive renal œdema. Plasma hypotonicity commonly complicates the course of long-continued anuria and oliguria. Unless sodium is lost by some extrarenal route (vomiting or diarrhœa), the cause of the hypotonicity is water retention, and no obscure metabolic cause need be invoked to explain it.

The converse condition, plasma hypertonicity (high plasma-[Na] level) is explained by depletion of water, and usually retention of sodium chloride (Allott 1939, 1957).

Both hypo- and hyper-osmolarity of the body fluids are common metabolic disorders in hospital practice and, if severe, may cause acute symptoms, mostly cerebral, and even death. Hypo-osmolarity has been reviewed by Wynn and Rob (1954) and Danowski et al. (1955), and hyperosmolarity by Knowles (1956).

Application of Osmotic Prediction Formula to Management of Body-fluid Disorders

In assessing a patient's need of fluid, the osmotic prediction formula can be of great value. In this situation, unlike the experimental one, complete accuracy is not needed, and the problem may be simplified. For example, plasma-[Na] may be substituted for [B]; and an assumed value for total body water judged on clinical grounds, from the patient's weight, and if possible from evidence of recent change of weight, may be substituted for the directly determined quantity. The working out of a few examples will show that useful estimates of fluid requirements can be obtained in this way. The following examples are from actual cases:

Example 1.—A man with mild concussion was admitted to hospital, where it was not known that he also had diabetes insipidus. He seemed to be making good progress at first but after two days he became irrational, noisy, and drowsy, and finally lapsed into coma. He had muscle twitching, overactive reflexes, extensor plantar responses, and pyrexia, and was overbreathing. At first an intracranial complication was diagnosed, but later it was noticed that he was passing large volumes of dilute urine, although his fluid intake had been small. Plasma-electrolyte estimations showed that the plasma-[Na] level was 165 mM per litre. Depletion of water and diabetes insipidus were diagnosed, and treatment was planned accordingly.

Calculation for Treatment

Before his accident the patient weighed 70 kg. and was not obese. Taking an average figure for total body water in lean males (60% body-weight), his normal total body water would be about 42 litres. Assuming that his initial plasma-[Na] was normal (140 mM per litre), and ignoring the urinary electrolyte loss (which would normally be small in these circumstances), the total body water (W_2) estimated from the simplified prediction formula would be 35·6 litres ($W_2 = \frac{140 \times 42}{165} = 35{\cdot}6$ litres). There was therefore a deficit of 6·4 litres of body water. To restore the patient's plasma-[Na] to normal, this deficit of water would have to be made good, bearing in mind the continuing losses of water from lungs and skin and in the urine, the volume of which was brought to normal by injection of antidiuretic hormone.

If the initial estimate of 42 litres of total body water was wrong by ±10%, the error in the calculated deficit of water would also be about 10%, and this would be of no clinical importance.

Treatment and Progress

Treatment was planned to restore the plasma-[Na] level to normal in forty-eight hours by the infusion of 5% glucose in water, 1 litre daily being allowed for insensible loss of water and 1·5 litres daily for urinary excretion. 50 mM of KCl was given daily as well. At the end of this time the patient was improved, but his plasma-[Na] was 150 mM per litre on duplicate analyses. Since this value was far from the expected one (140 mM per litre), the treatment was checked, and it was found that 3 litres of 5% glucose in isotonic saline solution (465 mM NaCl) had inadvertently been infused instead of the equivalent volume of 5% glucose in water. This error would explain very well the observed plasma-[Na], since this predicts a cation balance (bB) of + 426 mM. ($bB = (150 \times 42) - (165 \times 35{\cdot}6) = +426$ mM). Further treatment in this case was planned to keep total body water unchanged but to remove NaCl, which was done with an injection of mersalyl, which produced a good sodium-chloride diuresis.

This case illustrates how depletion of water may be assessed, the need of fluid estimated quantitatively, and treatment controlled by estimation of the plasma-[Na] level and by the (simplified) osmotic prediction formula.

Example 2.—A woman developed infective hepatitis and rapidly lapsed into deep hepatic coma, which lasted twelve days and then gradually lightened, with ultimate recovery. Her daily volume of urine while she was in deep coma was about 600 ml., although her daily intake of fluid during the twelve days was about 3000 ml., consisting of hypertonic glucose, 30 mM of NaCl, and 50 mM of KCl. The question arose whether there was any danger of overhydration in view of the consistent large discrepancy between intake and output of fluid. This was simply answered by the fact that the plasma-[Na] remained remarkably constant at about 140 mM per litre for the whole of this period. Dilution of the body fluids by excess water was therefore excluded, and the small intake of electrolytes excluded the possibility of significant retention of isotonic fluid. The apparent discrepancy in the fluid balance must have been due to unusually large insensible losses in the patient.

This is an example of how the plasma-[Na] level may be used to assess the water balance when the insensible loss is high. The plasma-[Na] may be used where the need of water is difficult to assess—e.g., in anuria, respiratory failure, and cardiac failure.

Example 3.—A woman with mitral stenosis but no œdema underwent mitral valvotomy uneventfully. On the fourth postoperative day she was excessively drowsy and weak and suddenly had a short generalised fit, followed by prolonged coma and overbreathing. There were no localising neurological signs to suggest cerebral embolism. Her plasma-[Na] level, normal preoperatively, was now 115 mM per litre. Fluid balances showed that the postoperative intake of electrolytes was nil, and that, when the usual allowance was made for insensible loss of fluid, the intake of fluid was only moderately in excess of the output. Thoracic drainage was 1·5 litres of serous fluid, and 3 litres of urine had been

passed since the operation. The presumptive diagnosis here was acute water intoxication.

Assessment

Initially the total body water was about 30 litres (50% of body-weight being the average figure for lean females) and the plasma-[Na] 140 mM per litre. The loss of electrolytes would be at least 200 mM of Na (in the serous drainage), and the same loss of K would be a reasonable estimate for the urinary excretion of cation after such major trauma. The cation balance was therefore about −400 mM, and the positive water balance (ΔW) was about + 3 litres.

$$(W^3 = \frac{(140 \times 30) - 400}{115} = 33 \text{ litres} \therefore \Delta W = +3 \text{ litres})$$

Treatment

Since urgent treatment was needed to avert further fits, hypertonic saline solution was infused in an amount calculated to raise the plasma-[Na] level to a safe value—i.e., 130 mM per litre—within twelve hours. In view of the danger of overloading the circulation with fluid, correction of the hypotonicity was planned so as to cause the minimum possible further increase in volume of the extracellular fluid. It was thought that in twelve hours the loss of water from insensible sweat and in the urine would be about 1 litre, the urinary excretion of sodium negligible, and the urinary excretion of potassium about 40 mM. The amount of NaCl necessary to produce the desired change in plasma-[Na] level was calculated to be 405 mM. (bB (Na + K) = (130 × 32) − (115 × 33) = 365, since K = −40, Na = 405). The NaCl was infused into a large vein as 5·85% NaCl (1 mM NaCl per ml.) to a total of 405 ml. The infused water (405 ml.) would mean that the desired negative water balance of − 1 litre would probably not be achieved, but this would not have an important effect in the calculations and was ignored for simplicity. However, if a less concentrated saline solution had been given (e.g., isotonic saline), or if the patient had been allowed to take fluids by mouth, the whole purpose of the treatment would have been largely lost and dangerous overhydration produced. The failure to control this aspect of treatment (the intake of water) explains many therapeutic failures in the treatment of hypotonicity due to water retention.

Subsequent treatment consisted of further gradual depletion of water and the infusion of 100 mM of KCl in twenty-four hours for some days to replace the potassium deficit and to restore the plasma-[Na] level to normal. Potassium was not infused while the plasma-[Na] was very low, because of the danger of hyperkalæmia in this situation (Laragh and Capeci 1955).

If the estimated quantity of total body water (33 litres) was wrong by ± 10%, the derived sodium balance calculated to correct the hypotonicity would be wrong by about the same amount. The effect of this inaccuracy on the predicted plasma-[Na] level would be an error of about ± 1·5 mM per litre, which is of no clinical importance.

These examples illustrate briefly how simple osmotic principles may be used to assess body-fluid disturbances and to prescribe for their treatment, in an approximately quantitative way. Correction of osmotic disorders is, of course, only one aspect of fluid therapy, but the others are beyond the scope of this paper.

Successful application of the osmotic prediction formula depends on reliable fluid-balance records and accurate biochemistry. Modern methods of analysis of the required accuracy are now generally available. The best work, however, cannot be expected if excessive demands for biochemical determinations are made on the laboratory; and several clinical biochemists, with whom I have discussed the problem, believe that this danger exists already.

The principles of management outlined here can help in two ways: (1) fluid therapy based upon physiological principles can prevent serious body-fluid disorders, and provide a sound basis for prompt treatment of those which have already arisen, and (2) when the biochemical results are clearly at variance with the results expected on clinical grounds, both the treatment and the biochemistry should be checked. In this way errors in either will be detected promptly and further difficulties, caused either by wrong biochemistry or by wrong treatment, can be avoided.

Summary

The question considered here is how tissue cells as a whole respond to acute changes, produced over twenty-four hours, in the body's content of water and osmotically active solutes (the electrolytes). Since unsolved technical problems preclude direct methods of answering this question, an indirect method is used, based upon studies of the composition of the extracellular fluid, from which the behaviour of the cells may be inferred.

The simplest view of the osmotic adjustments of body cells is that they respond to osmotic changes as if they were perfect osmometers. Given such behavour, an osmotic formula can be derived which enables the hypothesis to be tested. The test consists in producing a measured change in the body's water and electrolyte balance, observing the change in extracellular osmolarity (total ionic concentration), and comparing this value with the value predicted by the osmotic formula.

This comparison between the predicted and observed changes in extracellular osmolarity was made in 65 experiments in 26 patients. The osmotic stress consisted in changes (in various combinations) in the body's water balance and in the balance of sodium and potassium salts. Most of the subjects were studied during recovery from or treatment of established body-fluid disorders.

The results show that the observed and predicted changes in extracellular osmolarity agree within the limits of experimental error. Since other investigators have not found such agreement and consequently have postulated modes of osmotic behaviour other than the one which the present results support, the possible reasons for this disagreement are briefly discussed.

The practical value of this investigation lies in the greater certainty with which the estimation of plasma-electrolyte levels may be used in the management of certain body-fluid disorders. The total ionic concentration of the plasma, for which the plasma-Na level serves as an approximation, accurately reflects acute changes in water and electrolyte balance (hyperglycæmia excepted), and the converse applies.

The pathogenesis of body-fluid disorders involving changes in plasma osmolarity (the hypotonic and the hypertonic syndromes) is discussed in relation to these principles. The hypotonic syndrome is often due to retention of water and loss of potassium, and the hypertonic syndrome to depletion of water and retention of sodium chloride.

Examples are given, from actual cases, of how the osmotic prediction formula, simplified to make it readily applicable to clinical problems, may be used to make approximately quantitative assessments of the water and electrolyte imbalance and of the fluid therapy necessary to correct these.

A brief account is given of the application of these principles as an internal check on fluid-balance therapy and on the accuracy of the biochemistry. Significant errors in either will be reflected in an obvious discrepancy between the predicted and the observed extracellular osmolarity measured by estimating the plasma-Na level. The identification and elucidation of such errors will decrease the incidence of significant disorders of body fluid, speed the treatment of those which occur, and ultimately lessen the demands on the laboratory for unnecessary determinations of electrolytes.

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(*references overleaf*)

INFANTILE GASTROENTERITIS

CHANGING NEEDS IN TREATMENT

E. H. BROWN
D.M. Oxon., M.R.C.P., D.C.H.
ASSISTANT PHYSICIAN, HITHER GREEN HOSPITAL, LONDON, S.E.13

E. H. BAILEY
M.R.C.S.
PATHOLOGIST, SOUTHERN GROUP LABORATORY, HITHER GREEN, LONDON, S.E.13

THE relationship of certain serologically distinct types of *Escherichia coli* to infantile gastroenteritis has been firmly established since the original work by Bray (1945). and Giles and Sangster (1948). The number of types recognised as pathogens has steadily increased; they are rarely found in patients over the age of 2 years, and even more rarely can they be said to cause gastroenteritis over this age.

We describe here our experiences during the period 1952–56. Only children under 18 months are considered; few patients with diarrhœa and vomiting due to *Esch. coli* were older than this.

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Layout of the Unit

The gastroenteritis unit consists of 10 cubicles in a ward of 27 cubicles. No child under the age of 2 years is admitted to this ward unless thought to have infantile gastroenteritis. Each cubicle has its own wash-hand basin and supply of gowns. All soiled linen and napkins are put into bins and are not sorted on the ward. After handling a patient, the nurses and doctors disinfect their hands by immersing them in 1/80 benzalkonium solution for half a minute before washing under running water with soap. Small hand-towels are used (once only) to dry the hands. No nail-brushes are used, for strains of *Esch. coli* were isolated from them several times.

Bacteriological Diagnosis and Investigation

Irrespective of the clinical diagnosis, samples of the stools of all children under the age of 2 years admitted to the hospital were cultured on MacConkey's medium, and desoxycholate-citrate agar and in selenite F broth. Except where shigellæ or salmonellæ were found on desoxycholate citrate medium (with or without passage through selenite-F broth), the few non-lactose-fermenters isolated were either proteus or, occasionally, members of the paracolon group.

Single colonies from the MacConkey's agar were emulsified in saline on a slide and a loopful of 1/500 acriflavine solution was added. Absence of any auto-agglutination indicated that the colony was smooth. A loopful of pooled OB sera was then added. If the suspension was agglutinated, portions of colonies were tested against the individual members of the pool by placing small drops of the appropriate OB sera on a slide and emulsifying the organisms in them with a straight wire and observing the results with a plate microscope. Positive slide-agglutinations were confirmed to titre by scraping some of the growth from the plate into formol-saline, heating in a boiling-water bath for thirty minutes, and putting the suspensions up against the particular O serum in a 56° C water-bath for four hours.

Confirmation of the O antigen to titre was applied only when an organism was isolated for the first time in a patient. Organisms isolated subsequently were assumed to be the same from positive OB serum slide-agglutinations.

Sensitivity tests to antibiotics were done on MacConkey's agar using Evans' tablets.

Specific Serotypes and Other Smooth Strains of Esch. Coli

In 1952 only 4 types of *Esch. coli* were routinely investigated. By the end of 1956 the number had increased to 10 (O 26, O 55, O 86, O 111, O 114, O 119, O 125, O 126, O 127, and O 128). During 1952–56, 550 children under 18 months (excluding cases later found to have shigella or salmonella infections) were admitted to the unit. In 237 of these the illness was due to known pathogenic types of *Esch. coli*. In addition, with the increase of the number of types recognised as potential pathogens, it was decided in 1954 to record all cases where stool examination in a clinical case of gastroenteritis gave a pure growth of smooth *Esch. coli* which were not typable by the sera at our disposal but which,

TABLE I—NO. OF CASES OF INFANTILE GASTROENTERITIS DUE TO SEROLOGICALLY DISTINCT STRAINS OF *Esch. coli*.

Year	Strain												
	O 26	O 55	O 86	O 111	O 119	O 125	O 126	O 128	O 127	O 114	Total	"Smooth coli" (not typeable by our sera)	Total (known serotypes + "smooth coli")
1952	1	22	1	20	*	*	*	*	*	*	44	*	44
1953	1	23	8	10	1	2	*	*	*	*	45	*	45
1954	5	21	4	7	3	4	2	12	*	*	58	17	75
1955	6	24	1	2	9	7	1	10	*	*	60	27	87
1956	4	8	1	3	5	3	1	2	3	0	30	17	47
Total	17	98	15	42	18	16	4	24	3	0	237	61	298

* Type not investigated during that year.

TABLE II—NO. OF CASES OF INFANTILE GASTROENTERITIS ACCORDING TO AGE (KNOWN SEROTYPES ONLY)

Year	Total	Age		
		Less than 6 months	6–12 months	12–18 months
1952	44	25	14	5
1953	45	24	14	7
1954	58	35	17	6
1955	60	29	20	11
1956	30	22	7	1
Total	237	135	72	30

nevertheless, might be considered potential pathogens. In 1954–56 there were 61 such cases.

Except in 1956, the incidence of *Esch. coli* O 55 remained relatively constant, but there was a notable decline in the incidence of type O 111 (table I.) The age-distribution of patients with the known serotypes is shown in table II.

Treatment

Rehydration

Few patients needed intravenous fluids. Even in these the use of antibiotics enabled oral feeding to be started early, and intravenous therapy, using 2·5% glucose in 0·3% sodium-chloride solution, could usually be discontinued after thirty-six hours. Serum-electrolyte estimations were thus unnecessary. Subcutaneous fluid with hyaluronidase is of little value if dehydration is severe, because the associated peripheral vascular failure hinders absorption by this route. It was used only in borderline cases.

Feeding

All patients not needing intravenous fluids were given 2·5% glucose in 0·3% sodium-chloride solution by mouth during the first twenty-four hours. With satisfactory progress, half-cream National dried milk at half strength was introduced; it was increased to full strength usually by the end of a week. The return to a full-cream milk was somewhat slower, as fat is not well tolerated in the early stages. Special milks were very rarely needed. Sweetened condensed milk, given for a short time, was of value in starting a gain in weight in the few marasmic cases. Dried milks were used predominantly in this unit, but it is possible that unsweetened condensed milk will be used more frequently in the future.

Breast-fed Infants

Infantile gastroenteritis due to *Esch. coli* may (contrary to popular belief) arise in a breast-fed baby, but no severe case has ever been seen in this hospital. On no account should these babies be weaned from the breast, and most can be adequately dealt with at home. An investigation of the incidence of *Esch. coli* infection as a cause of mild diarrhœa in breast-fed babies would be worth while.

Antibiotics

The use of antibiotics has revolutionised the treatment of infantile gastroenteritis, even allowing for a decline in the severity of the disease. A first-class laboratory service is essential for a gastroenteritis unit. Stools must be sent for culture before treatment is started and sensitivity tests carried out in all cases. Many patients need treatment before the results are available. The antibiotic is then chosen in the light of previous experience. In this series strains of *Esch. coli* were rarely resistant to antibiotics (except streptomycin). Unusual sensitivity-patterns have been of interest in cross-infection studies but so far have not caused serious difficulties, though they may in future. (Sulphonamides proved to be ineffective and were not used during this period.)

Streptomycin was rarely used; for we, like others, found that many strains were resistant to it on admission, or rapidly became so (Alexander et al. 1952).

Chloramphenicol was used extensively from 1950 to 1952, but was discontinued when other antibiotics became freely available. It was effective and easily administered in the form of 'Chloromycetin Palmitate'. Agranulocytosis developed in 1 child, who recovered.

Aureomycin was used a little, chiefly in 1953. The gastro-intestinal side-effects were troublesome.

Oxytetracycline was the antibiotic of choice in 1953–56. Gastrointestinal side-effects were not troublesome and resistant strains rare.

Tetracycline was used in a few cases in 1956; gastro-intestinal-side effects were probably fewer than with aureomycin.

Neomycin was used only in the latter part of 1956. It is too early to assess whether it will prove superior to oxytetracycline, but it is not absorbed from the bowel and side-effects are few.

We believe that the antibiotic should be chosen from the last three. It should be given in doses of 50 mg. per kg. body-weight per day, in six-hourly doses for five days. A convenient, but rougher, dosage is 200 mg. a day for children under 6 months of age and 400 mg. a day for those over 6 months. In the few cases where intravenous fluids are needed, enough fluid is allowed by mouth to administer the antibiotic, and no difficulty has been experienced.

It is not suggested that all patients with infantile gastroenteritis due to *Esch. coli* should be given antibiotics. Some cases are very mild and need little more

TABLE III—NO. OF SEVERE CASES (NEEDING INTRAVENOUS FLUID) AND TYPE OF *Esch. coli* (INCLUDES 4 CASES OF CROSS-INFECTION)

Year	No. of cases	Type of *Esch. coli* isolated	Deaths
1952	15	O 111 (7) O 55 (8)	1
1953	9	O 55 (6) (1 cross-infection) O 111 (3) (1 cross-infection)	1
1954	7	O 111 (2) O 128 (4) (2 cross-infections) " Smooth coli " (1)	1
1955	4	O 55 (1) O 125 (1) O 128 (1) " Smooth coli " (1)	1
1956	2	O 111 (1) " Smooth coli " (1)	0

than preliminary starvation followed by graduated feeds. Moderate or severe cases must be treated with antibiotics, and the response is rapid. Within twenty-four or forty-eight hours vomiting is controlled, diarrhœa has lessened, and the child can tolerate dilute milk feeds. Subsequent progress is usually uneventful, though sometimes the stools are slow to return to normal. The child may relapse within ten days after treatment has been stopped, but relapses are not usually severe. Many so-called relapses in the past were due to cross-infection, and this has become more apparent as the number of known pathogenic strains of *Esch. coli* has increased.

Grades of Severity

It is hard to obtain any uniformity in the grading of cases. By *severe* is implied those cases which required intravenous fluid for rehydration. The incidence of these cases declined strikingly during the five years (table III). In addition, since 1950 the use of antibiotics has resulted in rapid improvement of cases with early dehydration on admission and enabled rehydration to be achieved by oral administration of fluids.

Deaths

Of the 550 patients 4 died ; 3 of them were among the 237 cases due to *Esch. coli*. They were all aged 3 months or less, and there were other contributory factors :

Case 1 (1952).—A boy aged 9 weeks was marasmic and severely ill on admission ; he had been cross-infected with *Esch. coli* O 55 at another hospital. Response was poor despite antibiotics and intravenous fluids. He had several relapses and his condition gradually deteriorated.

Case 2 (1953).—A child, aged 2 months, had gastro-enteritis due to *Esch. coli* O 111. There was an associated large meningomyelocoele with complete paraplegia, and treatment was not, perhaps, pressed as vigorously as usual.

Case 3 (1955).—A child, aged 3 months, had gastro-enteritis due to *Esch. coli* O 55. He was severely ill but responded initially to oxytetracycline. Later, paralytic ileus and bronchopneumonia developed. Necropsy showed many gram-positive cocci in the lungs, but unfortunately no culture was taken. Death may have been caused by staphylococcal septicæmia resistant to oxytetracycline.

Case 4 (1954).—A child whose diarrhœa on admission was due to fibrocystic disease of the pancreas was later cross-infected with *Esch. coli* O 86, O 119, and O 128.

Course of Illness

Incidence of Cross-infection

There is a high incidence of cross-infection with *Esch. coli* in a gastro-enteritis unit (Anderson et al. 1954, Jameson et al. 1954, Rogers 1951), and indeed in any type of ward to which children under 2 years of age are admitted. These types of *Esch. coli* can survive outside the body for long periods. In the early stages very many organisms are present in the stools and sometimes in the vomitus. At this stage the case is most infectious. Well-trained and reliable nurses are essential ; but, even with the strictest cubicle isolation technique, some cross-infection seems almost inevitable. The contamination of the whole cubicle in the acute phase probably explains why insistence that " the nurse who changes the babies does not feed them " has not proved very helpful.

Nearly half the cases of proved cross-infection (table IV) were in children admitted with a history of diarrhœa and vomiting, but in whom no pathogenic strains of *Esch. coli* were isolated (table IV). In these an acute attack of gastroenteritis developed later, and stool-culture then showed a pure growth of a strain of *Esch. coli* known to have been present in the unit at that time. 20 other patients had been cross-infected in pædiatric units elsewhere—often by children (admitted for other reasons) who were symptomless carriers of pathogenic strains of *Esch. coli*. In this hospital in 1952–56, there were 36 known cases of cross-infection with *Esch. coli* gastroenteritis among children under 18 months admitted for other conditions to wards other than the gastro-enteritis unit. Most of the cases were seen before 1954 in the ward for whooping-cough—the only open ward where there are many children of this age-group. Fortunately, these illnesses were not, for the most part, severe. With early treatment all patients recovered. Since 1955 examination of fæces on admission has been the rule for all children under 2 years admitted to open wards. If a symptomless carrier is found he is transferred to the gastroenteritis unit. Since that time, cross-infection in the whooping-cough ward has been negligible. More recently, stools have been examined as a routine in the other cubicle ward where cross-infection from symptomless carriers may occasionally arise.

TABLE IV—NO. OF CASES OF CROSS-INFECTION WITH *Esch. coli* IN THE GASTROENTERITIS UNIT

Year	*Esch. coli.* isolated on admission ; cross-infection with different strain	" Smooth coli " only on admission ; cross-infection with known serotypes	No cause found on admission ; cross-infection with known serotypes	Total	No. of children at risk
1952	3	..	5	8	93
1953	6	..	9	15	93
1954	10	0	4	14	111
1955	4	0	2	6	136
1956	2	3	2	7	117
Total	25	3	22	50	550

Contamination of feeds during preparation does not cause much cross-infection in a gastroenteritis unit, but it is one of the few factors that can be easily eliminated.

The feeds should not be made up by a nurse handling the babies, and a central milk kitchen is desirable ; we have had one only since early 1957. An alternative is for all the feeds to be made up for the twenty-four-hour period, the teats put on and covered with a loose metal cap, and the batch then autoclaved. It has been found satisfactory to bring the pressure up slowly to 10 lb. per sq. in. and then allow the batch to cool. The process takes about thirty minutes. The feeds are then stored in the refrigerator until needed. On no account should the teat be handled before feeding, unless this is essential.

Duration of Stay

The duration of stay in hospital is a poor index of the severity of the illness, because it depends largely on social factors and cross-infection. Many of the infants come from institutions and nurseries and cannot therefore be discharged until the stools are free of pathogens. After treatment about 15–20% of patients still have positive stool-cultures, though the majority do not get a clinical relapse and can be discharged if they come from their own homes. In the 237 cases due to known pathogenic strains the average durations of stay were as follows : 1952, 34 days ; 1953, 32 days ; 1954, 27 days ; 1955, 22 days and 1956, 19 days. The main factors contributing to this progressive fall in the duration of stay were a more vigorous policy of early discharge of patients coming from their own homes, a somewhat lower incidence of cross-infection, and a decline in severity of the disease.

Other Causes of Diarrhœa and Vomiting

Of the 252 children under 18 months of age admitted to the unit during the period, in whom no pathogenic strains of *Esch. coli* or shigella or salmonella were isolated, no specific cause could be found in most. Their illnesses were, for the most part, mild and cleared up in a few days. In this group, admission to hospital could not be justified in many cases from the history, the clinical examination, or the social circumstances. It is unusual, in a gastroenteritis unit, to find many cases of such parenteral infections as otitis media, pneumonia, and pyelitis, which, as causes of gastroenteritis of infants, tend to have been exaggerated in many textbooks. Meningococcal infection is an important but rare cause. Some of the mild cases appear to be associated with the eruption of a tooth.

Conclusions

Infections with various pathogenic strains of *Esch. coli* are the cause of the majority of cases of infantile gastroenteritis. The severity of the disease has lessened. The use of antibiotics has revolutionised its treatment, which is now relatively simple in most cases. The mortality is low. Cross-infection in gastroenteritis units remains high and is unlikely to be eliminated. These facts demand that our ideas on the management of such cases should be reorientated.

Ten years ago, when severe cases were common and treatment difficult, there was every justification for admission to hospital. Now, of patients living in their own homes, only the severely ill should be admitted to hospital ; the others should be treated at home. Stools should be sent to a laboratory, and antibiotics used,

if the clinical condition warrants it, before the results are available. In most cases, there will be no other children of a susceptible age-group (i.e., under 2 years) in the family. If there are, they have probably been cross-infected by the time the first patient is seen by the doctor.

Many patients have to be admitted because they come from residential nurseries and institutions (especially rest-centres), which are becoming a permanent feature of our national life. In addition, housing conditions may be bad enough in some cases to render home-nursing impossible. When the mother has to work to support the family, financial help should be given. This would certainly be less expensive than admission to hospital and would be in the best interests of the child.

In hospital strict cubicle-isolation technique will limit the amount of cross-infection. Gastroenteritis units should be small; if the number of positive cases is high at any one time, cross-infection is especially likely. In these circumstances a unit of even 10 beds in one ward may be too large. Although negative stools are necessary before discharge of patients coming from institutions, patients from their own homes should be discharged as soon as possible. Discharge should not be delayed on account of positive stools if there are no symptoms. Furthermore, if the mother is capable, it has been the policy of this unit to allow children under 6 months to go home on half-cream feeds. The change-over to normal feeding is made gradually at home away from the dangers of cross-infection.

A patient with mild illness, treated at home, may not need antibiotics, though he will in hospital because he is a source of cross-infection. *If a patient is admitted to a gastroenteritis unit and the diagnosis of gastroenteritis is not confirmed, he should be removed immediately.*

Stool-cultures should be made for all children under 2 years admitted to hospital, irrespective of the diagnosis, and symptomless carriers removed from the ward. It is not very satisfactory to send them to a gastroenteritis unit, for they may be cross-infected with a strain foreign to them and develop an acute attack. It would be preferable to send them to a small cubicle unit attached to an adult ward.

There is no satisfactory explanation for the decline in the severity of infantile gastroenteritis in the London area in recent years, but similar cycles of virulence are seen in other diseases. It has been suggested that, in the case of O 111, decline in virulence has been associated with a change in the H antigen (Smith 1954). The H antigen has not been routinely investigated in this unit, and the figures are too incomplete for comment on this.

Summary

237 patients with infantile gastroenteritis due to serologically distinct strains of *Esch. coli* were admitted to the unit in 1952–56. In 61 cases of clinical gastroenteritis a pure growth of smooth *Esch. coli* was obtained from the stool but was not typable with the sera available.

4 babies died. Other contributory factors were present in these cases.

Where antibiotics are indicated, the choice seems to be between oxytetracycline, tetracycline, and neomycin. The use of antibiotics has greatly simplified treatment. Intravenous fluids are not often needed.

The incidence of cross-infection was high.

The decline in severity and ease of treatment demands a change in approach to the management of cases. Children under 2 years of age with diarrhœa and vomiting should not be admitted to hospital unless the clinical condition or social circumstance demand it.

Although, in the London area, the disease is not at present serious, it may become serious. Only constant vigilance can ensure that children under 2 years of age, necessarily admitted to hospital, are not exposed to needless risks.

We are indebted to Dr. L. J. M. Laurent for his helpful criticism and advice; thanks are also due to other colleagues who have assisted in the unit during this period.

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Occasional Survey

RESEARCH AND MENTAL DEFICIENCY*

BRIAN H. KIRMAN
M.D. Lond., D.P.M.
CONSULTANT PSYCHIATRIST AND DEPUTY MEDICAL SUPERINTENDENT, THE FOUNTAIN HOSPITAL, LONDON

MENTAL retardation—including certified mental defect, cases under supervision of various forms in the community, and educational subnormality, dullness, and backwardness—is perhaps the commonest of all forms of handicap; but little is known about its causes and little research is now being devoted to them. This may be partly explained by the very widespread view (Tredgold and Soddy 1956) that in over 70% of cases mental defect is due to genetic factors and that very little can therefore be done about it.

But Penrose (1938) emphasised the importance of environmental and social factors in every case of backwardness, and the attention of the general public has lately been aroused by the activity of voluntary bodies; and interest has increased in the research on the causation, prevention, and treatment of mental defect. The small amount of work already done indicates that social factors can have a striking effect on the prevalence of mental retardation, and in a few specific conditions it has been shown that medical treatment can at least partly correct the effects of faulty heredity.

* * *

The studies of the social psychiatry unit of the Medical Research Council show that, despite an elaborate system of ascertainment and complicated legislation, data about the prevalence and nature of mental defect are very limited. O'Connor and Tizard (1954), of that unit, showed that some 58% of patients in hospitals as mental defectives in Kent, London, and Surrey, were classed as feeble-minded (a figure which agreed very closely with a 1949 Board of Control census), and that these feeble-minded patients between the ages of 16 and 30 years, tested on the progressive matrices scale, had an average equivalent intelligence quotient (I.Q.) of 71–74. O'Connor and Tizard (1956) report similar findings of their own and of other workers at the Manor Hospital, using both the matrices and the full Wechsler-Bellevue scale. Other hospitals provide evidence that this is not unusual.

Thus there is a considerable overlap, in point of test performance, between mental defectives and the general population. There was little evidence of gross departure from accepted standards of stability of behaviour among the sample investigated. Elaborate tests for neuroticism proved unhelpful, and O'Connor and Tizard conclude that it is better to give an individual the chance of

* Based on a paper read at a meeting of the Royal Medico-Psychological Association on April 10, 1957.

rehabilitation rather than to reject him on the basis of such a test.

These results raise many questions as to the adequacy of our mental-deficiency services, and, with the recommendations of the Royal Commission on the Law Relating to Mental Illness, suggest that many of the more intelligent patients might be better treated by ordinary social agencies outside the scope of the mental-deficiency acts, and that short-term rehabilitation in small hostels may often be preferable to long-term stay in large institutions.

An equally searching review has been made of long-established beliefs concerning the learning-capacity of imbeciles. Gordon et al. (1955), O'Connor and Claridge (1955), and Walton and Begg (1955) have shown that imbeciles are very responsive to appropriate incentives, particularly to social approval, and that these are essential to prevent deterioration. With suitable training the performance of imbeciles at commercial tasks improved steadily, and many were capable, under sheltered workshop conditions, if not of earning their living, at least contributing to their keep. It is wrong to assume that defectives, because of low intelligence, should be left to do simple, uninspiring, and uneconomic tasks.

Another form of research which scrutinises accepted views is the study of children of mental defectives. In a survey carried out by M. W. G. Brandon (Hilliard and Kirman 1957), 150 children of 73 certified mentally defective mothers were studied: 6 were certified under mental-deficiency Acts and 4 were in schools for the educationally subnormal. Thus, 91% of the children alive at the time of the survey were regarded as normal individuals, despite the many additional difficulties to which the children of certified defectives are exposed. 66 of the 73 mothers (90%) are now living or working in the community and 26 are married. In this series the mother with the lowest I.Q. had the child with the highest I.Q., and vice versa. The mean I.Q. of the children was 91·3 (range 30–132).

Researches of this kind are likely to benefit most people in that they deal with the broader aspects of the subject, and should enable social and legal provision to be revised on a sound basis. Meanwhile, useful contributions have dealt with limited and specific parts of the field—e.g., studies of particular diseases causing mental defect. The review by Cowie (1951) of phenylketonuria added to our knowledge of this, the commonest metabolic disorder causing mental deficiency.

* * *

Advances in pædiatrics are reducing the total of mental defect, in particular by better treatment of conditions which damage the brain. There is still room for improvement, since in recent years 35 young children have been admitted to the Fountain Hospital with mental defect due to meningitis—tuberculous in 10 and septic in 25 (Kirman 1957).

Prematurity is an interesting subject for those concerned with mental defect. Douglas (1956), in a carefully controlled study, has shown that premature children on average do slightly but significantly less well on tests than others. There is an undue proportion of premature children among mental defectives. Crome and Williams have under review the cases of 25 children with retrolental fibroplasia, impaired vision, and mental defect.

Drillien and Richmond (1956) found a significant relationship between prematurity and illegitimacy. There was also a distinct correlation between prematurity and the Registrar-General's social classes, the prevalence in classes III–V being much higher than that in classes I–II. They also found that the prematurity-rate rose after the second birth in classes III–V, whilst I and II maintained their low prematurity-rate with all births after the first. In classes III–V the prematurity-rate rose to nearly 18% after the sixth birth. Drillien and Richmond conclude "that in the poorer homes every additional baby brings added financial strain and extra work and worry to the mother".

The analogy of stillbirth is particularly interesting. Crome (1954) studied 117 brains from low-grade mentally defective children and showed that in almost all such cases there was gross abnormality of the brain. There was clear evidence of some postnatal cause for the brain lesions in some cases, but in the majority the abnormality was such that it was probably already present at birth. Had these lesions been more severe the result might well have been stillbirth. Potter (1952), in his study of the pathology of the fœtus and of the newborn, points out that the commonest forms of fœtal pathology found were involvement of the central nervous system, with hydrocephalus, anencephaly, and spina bifida. Lissencephaly, macrogyria, porencephaly, cebocephaly, and many other brain deformities, are found in stillborn infants. It seems that, just as brain abnormality is associated with many deaths in the neonatal period, even more severe brain defects are commonly the cause of stillbirth.

It is tempting but unjustifiable to assume that in humans there is such a direct and simple relationship between dietetic inadequacy and fœtal pathology as Millen and Woollam (1956) found when studying hydrocephalus and shortage of vitamin A in rabbits. It seems likely, however, that nutrition is the biggest single factor accounting for the difference in incidence of stillbirth in the different social classes, and for the improvement in the stillbirth-rate in recent years (Leff 1953). If we accept this conclusion, then it seems logical to take a further step and assume that many of the severer forms of brain abnormality, and possibly also some of the minor departures from the normal which are seen in mental defect, are associated with indifferent nutrition, among other adverse factors affecting fœtal development.

It is hard to distinguish between the effects of a variety of potentially adverse factors which may be present in intra-uterine life. Stott (1957) found a relationship between what he termed "pregnancy stress" on the one hand and infantile morbidity and mental backwardness on the other. Under the term "pregnancy stress" he included such psychological factors as worry and such derangements of pregnancy as uterine bleeding. Both may be commoner when the environment for the pregnant woman is unsatisfactory, though Stott claims to have eliminated this by a rating of home circumstances. *Prospective* studies of these relationships are needed.

Bourne (1955) discussed the possibility of gross amentia due to "pathological mothering", and claimed to have established this cause in a few cases without known gross organic brain lesions. This claim merits further study, with independent assessment of the neurological status and of the early history.

It has been argued that, with general improvements in social provision the number of mental defectives will tend to increase, owing to a reduction in the infant-mortality rate, which was presumed to eliminate the unfit. But the considerations mentioned above suggest the opposite, and that any improvement in the health of the mother will tend to be reflected in the mental as well as in the physical development of the child. With certain causes of mental defect improved care in prevention of disease seems to more than outweigh the increase in the number of defectives resulting from keeping alive those who would otherwise have died. Thus, in rhesus incompatibility (Crome et al. 1955) most of the defective children studied had received treatment that would now be considered inadequate, and they might therefore not have been defective if suitably treated. It was only

towards the end of the period studied that a few patients were seen whose survival was due to treatment. Further advances might remove blood-group incompatibility altogether from the list of causes of mental deficiency—if, for example, the mother's anti-D antibodies could be absorbed some time before delivery; but research in this direction has so far given very limited results (Pickles 1949).

* * *

Recent years have seen an increasing realisation that mental deficiency is not an "all-or-none" phenomenon and that mental defectives merge with and overlap with the general population. Together with this has come a better understanding of the importance of environmental factors and an appreciation of the fact that in many cases multiple factors, not least of which are social and educational, are involved in producing mental retardation. This change has been accompanied by a more optimistic attitude towards rehabilitation and the prospects for the mental development of future generations. The results of the two Scottish surveys of 1932 and 1947 (Scottish Council for Research in Education 1949) tend on the whole to favour this optimism, showing that test performance in schoolchildren has not fallen off, and may even have increased slightly.

At the same time a much better understanding has arisen of the role of genetic factors in mental deficiency, particularly in regard to specific diseases causing mental deficiency. The very vague terms "neuropathic diathesis" and "stigmata of degeneration", which were based on subjective and often erroneous impressions, are gradually being replaced by objective measurement. Thus Cowie and Penrose (1951) showed that in phenylketonuria, in which important aminoacids are lost in the urine—as in Fanconi's syndrome, another form of aminoaciduria (Cowie 1956)—the hair of affected persons is lighter than that of their normal siblings. Similarly in gargoylism—another form of metabolic defect which is genetically determined—there are certain characteristic deviations from the normal in physical appearance; notably deformity of the head, kyphosis, and enlargement of the spleen and liver, with corneal opacities (Ellis et al. 1936).

As Garrod (1931) suggested, many of these more specific genetic factors, which account for a small proportion of all defectives, operate in the form of a definite enzyme-system defect. Emphasis has, therefore, increasingly shifted in research to a study of the precise nature of the metabolic error. Thus, it is now held that in phenylketonuria there is a failure of hydroxylation of phenylalanine. This leads to faulty formation of tyrosine and melanin, with consequent dilution of hair and eye pigment, and to an accumulation of unused phenylalanine and its breakdown products, such as phenylpyruvic acid, which is responsible for the green colour in the urine on the addition of ferric chloride. The present view is that this excessive accumulation of metabolites in the blood is responsible for faulty functioning of, and eventually damage to, the brain. Armstrong and Tyler (1955) and others have claimed that such patients do appreciably better when fed a diet low in phenylalanine early in life. Perhaps the brain is less likely to suffer permanent damage later in life, and if it can be protected in the first few years a strict diet may be less important later.

In some metabolic disorders resulting in faulty function of the brain, dietetic measures may help. Komrower et al. (1956) showed that children with galactosæmia remain mentally normal on a lactose-free diet, while cataracts already formed may disappear. Addition of lactose to the diet led to striking aminoaciduria after 5 days; this increased till the 10th day, when the lactose-free diet was resumed.

These special diets are hard to administer, and better results might be obtained in these metabolic errors (including perhaps the whole range of the lipoidoses) if a suitable replacement therapy could be devised, on the lines of insulin treatment for diabetes mellitus. But in such conditions as phenylketonuria there is a great variety of metabolites in excess (Boscott and Kirman 1955), and Ottaway (1957) concludes that metabolism of tyrosine is impaired as well as that of phenylalanine. If the metabolic pathways are blocked at more than one point, the discovery of suitable replacement therapy may be a complicated process.

Another development of great theoretical and practical interest is the increasingly frequent claims that the carrier-state can be identified in such recessive syndromes as the renal type of diabetes insipidus (Kirman et al. 1956) and phenylketonuria. Forssman (1955) and Carter and Simpkiss (1956) both claim to have discovered a lack of urine-concentrating power in mothers of the former group, while Hsia and Driscoll (1956) find reduced phenylalanine tolerance in phenylketonuria heterozygotes.

Against these promising developments one must set the possible increase in genetic predisposition to mental deficiency which may result from release of radioactive material. It is now well known (Plummer 1952, Yamazaki et al. 1954) that microcephaly may be produced by exposure of the mother after conception, but the genetic hazard is still subject to study. Crow (1957) has emphasised that in this connection there is no "safe dose", any increase in the "background radiation" being likely to cause unfavourable mutations. Little is known about the biological effects of radioactive strontium (Medical Research Council 1956) which constitutes a special hazard, and until further research has been done it cannot be assumed that the accumulation of this substance in the bones of children will not add to the risk to future generations.

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Public Health

POST-MORTEM FINDINGS IN 46 INFLUENZA DEATHS

C. GILES
M.D., B.Sc. Manc.
CONSULTANT PATHOLOGIST

EILEEN M. SHUTTLEWORTH
M.R.C.S., D. Obst.
REGISTRAR IN PATHOLOGY

CITY GENERAL HOSPITAL, STOKE-ON-TRENT

THE recent influenza epidemic spread to North Staffordshire during the second week of September, 1957. Schoolchildren were the first to be affected and the disease was initially not severe. By the end of the month, however, a large proportion of the adult population had become infected, and an increasing number of patients with pneumonia and other complications of influenza were being admitted to hospital. The epidemic reached its peak during the third week of October and declined rapidly thereafter.

It is impossible to assess the incidence of the disease in the general population and, therefore, to calculate the overall mortality. However, the case-fatality of patients admitted to hospital with pneumonia at that time exceeded 25% despite intensive antibiotic therapy. In addition, a number of patients with other diagnoses subsequently contracted influenza and pneumonia in hospital. In the City General Hospital, Stoke-on-Trent, there were altogether 53 deaths in which influenza or one of its complications was the principal or a contributory cause. Necropsies were performed on 2 further patients who had died at home.

41 patients were males and 14 females. The age-distribution was :

Age-group (yr.)	*No. of cases*	*Age-group (yr.)*	*No. of cases*
11–20	5	51–60	15
21–30	3	61–70	10
31–40	4	71–80	8
41–50	8	81–90	2

Necropsies were done on 46 patients, 35 male and 11 female. An analysis follows of the findings in this group. In 40 cases, influenza or one of its complications was held to be the primary cause of death, and in the remaining 6 it was a contributory factor. 35 cases, or 76%, showed pre-existing lesions which contributed in varying degree to death. The lesions were :

Lesion	*No. of cases*	*Lesion*	*No. of cases*
Chronic bronchitis and emphysema (either singly or jointly)	16	Myocardial fibrosis or infarction	5
Hypertension	9	Chronic nephritis and nephrosclerosis	4
Rheumatic heart-disease	7	Bronchiectasis	3
Pneumoconiosis	5	Diabetes	2*
		Others	6

* 1 associated with an oxyphil adenoma of the pituitary, and acromegaly.

Post-mortem Findings

Upper respiratory tract.—The lower half of the trachea and the main bronchi were inflamed in all but 2 cases. This inflammation varied from mild injection to ulceration and sometimes membrane formation. In 24 cases the larynx and nasopharynx were likewise involved. Microscopic examination in the more severe cases showed complete disappearance of the ciliated epithelium, which was replaced by inflammatory granulation tissue.

Pleural cavities.—Fibrinous pleurisy was found in 4 cases, small effusions in a further 6. Bilateral pneumothorax, due to multiple small staphylococcal lung abscesses, was found in a girl aged 11 years.

Lungs.—37 patients (79%) had pneumonic consolidation; bronchopneumonia was present in 13 and lobar pneumonia in the remaining 24 cases. Pulmonary œdema often accompanied pneumonia, and in 4 cases there was frank abscess formation. In several instances, microscopic examination revealed breakdown of alveolar walls with the formation of numerous small abscesses where this had not been apparent to the naked eye. The pulmonary alveoli were plugged with neutrophils and red blood-cells; their walls were often necrotic and the alveolar ducts were greatly dilated.

Heart.—Chronic rheumatic lesions were present in 7 patients. 3 of these had mitral stenosis, 2 a combination of aortic and mitral stenosis, and 2 mild mitral incompetence. Myocardial infarcts or scars were found in 5 cases, 2 of them in the rheumatic hearts, 2 others in elderly patients with coronary atheroma, and a 5th in a patient who had had a recent coronary thrombosis.

One of the most striking findings was the high prevalence of cardiomegaly. Taking into account the age and stature of the patient, 24 out of 34 men and 5 out of 10 women had cardiac enlargement. As seen in table I, chronic lung-disease, rheumatic carditis, and hypertension were present in all but 2 of these cases. In 13 cases both ventricles were hypertrophied, but only in 4 of these could associated lesions explain this bilateral hypertrophy. On microscopic examination the most constant finding was myocardial œdema.

1 patient, a man of 41, deserves special mention. He was admitted with five days' history of influenza, and was found to have congestive heart-failure and pneumonia; he survived for six days in hospital and remained normotensive throughout. At necropsy his heart weighed 595 g. with well-marked right-sided and moderate left-sided ventricular hypertrophy. Microscopic examination showed large numbers of neutrophils, eosinophils, and plasma cells infiltrating both the myocardium and an organising thrombus which lined the endocardium. There were no Aschoff nodes and no other evidence of rheumatism.

The spleen was hard and congested, and enlarged in many patients with terminal congestive heart-failure. 15 patients who died of severe toxæmia or fulminating pneumonia had a small soft spleen with an almost diffluent pulp.

The brain was congested in about a third of the cases.

2 patients were admitted in coma; in both a clinical diagnosis of acute encephalitis was made. At necropsy the brain in both cases was intensely congested and rather œdematous, but microscopic examination failed to show evidence of virus encephalitis. In another patient, a man of 52, who died of bilateral adrenal hæmorrhage, a generalised streptococcal meningitis was found at necropsy; this had arisen from an acute otitis media following influenza.

Œsophagitis was found in 2 cases.

TABLE I—ANALYSIS OF CASES WITH CARDIOMEGALY

Sex	Age (yr.)	Heart weight (g.)	Associated lesions	Side of cardiac hypertrophy
F	29	382	Rheumatic carditis	Right
M	45	445	,,	,,
M	32	498	,,	,,
M	42	500	,,	,,
M	21	610	,,	Bilateral
M	36	830	Rheumatic carditis and hypertension	Left
F	57	354	Chronic lung disease	Bilateral
F	53	420	,,	Right
M	67	423	,,	,,
M	55	430	,,	,,
M	62	438	,,	,,
M	61	444	,,	Bilateral
M	51	475	,,	Right
M	57	548	,,	Bilateral
M	70	590	,,	,,
M	41	595	,,	,,
M	40	835	,,	,,
M	71	575	Chronic lung disease and hypertension	,,
M	52	725	Chronic lung disease and hypertension	,,
F	60	335	Hypertension	Left
M	62	434	,,	,,
M	49	502	,,	,,
M	64	560	,,	Bilateral
M	74	578	,,	Left
M	42	590	,,	,,
M	25	535	Hypertension and chronic nephritis	,,
F	17	405	Pre-eclamptic toxæmia	Bilateral
M	43	523	None	,,
M	64	680	None	,,

TABLE II.—SENSITIVITY TO ANTIBIOTICS OF 14 STRAINS OF *Staph. aureus*

Phage type	Sensitivity to						
	Penicillin	Streptomycin	Chloramphenicol	Erythramycin	Tetracycline	Novobiocin	Bacitracin
–	–	+	+	+	+	+	+
29	+	+	+	+	+	+	+
54/77	+	+	+	+	+	+	+
3A/3C/7/42E/75 +	+	–	–	–	–	+	–
29W	+	+	+	+	+	+	+
75/420	–	–	–	+	–	+	+
6/7/47/53/54	–	+	+	+	+	N.T.	+
75/77	–	–	–	+	–	+	+
75/77	+	–	–	+	+	+	+
75/77	–	–	–	+	–	+	+
54W/29/54/70/77	+	+	+	+	+	+	+
75/77	–	–	–	+	–	+	–
52/52A/79	–	+	+	+	+	+	+
6/47/54 +	–	–	+	+	–	+	+

+ sensitive. – resistant. N.T. not tested.

Kidneys.—Chronic glomerulonephritis was found in a man aged 25 and nephrosclerosis in 3 cases.

Finally, in a girl aged 17, who had been admitted with influenza and pre-eclamptic toxæmia, pneumonia developed in hospital, and she died two days later during the first stage of labour. Her kidneys were œdematous, with cortical pallor. On microscopic examination the glomeruli were œdematous and relatively avascular. There was no sign of infection in the fœtus. Influenza virus was not recovered from the lung of mother or fœtus, nor from the amniotic fluid.

Bacteriological and Virological Examination

All patients had been treated with antibiotics immediately on admission. Most received chloramphenicol; in a number this was supplemented by combined penicillin and streptomycin or by erythromycin.

Despite intensive drug therapy, *Staphylococcus aureus* was isolated from the lungs or bronchi in 15 necropsies. In 14 of these there was pneumonia, with multiple lung abscesses in 2. The sensitivity of 14 strains to the commoner antibiotics was determined (table II). 6 strains were sensitive in vitro to the antibiotic with which the patient had been treated, but in 5 of these cases death had supervened within forty-eight hours of admission. 12 strains were phage-typed. Type 75/77 was found in 4 strains with a similar antibiotic sensitivity pattern; otherwise there were no common phage types.

Other pathogenic organisms isolated post mortem were pneumococci (5 cases), non-hæmolytic streptococci (4), *Klebsiella pneumoniæ*, *Hæmophilus influenzæ*, *Pseudomonas pyocyanea* (each isolated once), and *Candida albicans* (isolated from 1 lung and the 2 cases of œsophagitis).

Lung specimens from 14 cases were examined by Dr. E. M. Mackay-Scollay at the public-health laboratory, Stafford, for the presence of influenza virus. Influenza-A virus of the Asian type was isolated from 8 of these; in 4 of them no bacterial pathogens were found, but the remainder also yielded *Staph. aureus*.

Discussion

Although the overall mortality in the recent influenza epidemic must have been relatively low, there has been a high case-fatality in hospital patients from pneumonia and other complications. Patients with chronic chest diseases, hypertension, and rheumatic carditis appeared to be specially vulnerable. The necropsy appearances of the respiratory tract confirm previous descriptions (Wolbach and Frothingham 1923, Straub 1937, Wollenmann and Finland 1943, Baker-Bates 1951). The high prevalence of cardiomegaly may simply mean that patients with enlarged hearts due to hypertension, rheumatic heart-disease, and chronic chest disease are more liable to get pneumonia and to succumb to toxæmia. On the other hand, the size of the heart was often greater than underlying conditions would have led one to expect, and in 2 cases there was no apparent cause. It is also unlikely that pre-existing hypertension had been masked by early peripheral failure in a large proportion of cases, since there was no microscopic evidence of that. Although Wood (1941) found no sign of myocarditis in a large series of deaths during the influenza epidemic of 1936–37, there was at least 1 case of acute myocarditis in our series. Cardiac enlargement may sometimes have been produced or enhanced by acute myocardial œdema due to toxæmia, and this may also have been the direct cause of death.

The most common bacterial pathogen was *Staph. aureus*, but neither phage-typing nor the antibiotic-sensitivity patterns suggested a predominant strain. Our inability to isolate *H. influenzæ* (except in 1 case) and any bacterial pathogens at all in 21 cases, may in part be due to the effect of antibiotic therapy, though in many instances treatment had not been given for more than twenty-four to thirty-six hours before death. It is, therefore, possible that in many cases pneumonia and death were the direct result of infection by the influenza virus.

Summary

Post-mortem examinations were performed on 46 patients who had died of influenza or a complication of influenza.

Of 35 men and 11 women most were aged between 41 and 75.

Pneumonia was found in 37 cases and pre-existing disease in 35. Chronic lung disease, rheumatic carditis, and hypertension were the commonest pre-existing diseases. 29 patients had cardiac enlargement, which could only in part be explained by chronic heart-disease or lung disease.

Influenza-A virus, Asian type, was isolated in 8 out of 14 lung specimens examined. *Staphylococcus aureus* was recovered at 15 necropsies; a common phage type was not encountered. *Hæmophilus influenzæ* was isolated in only 1 case.

At least 1 case of myocarditis was found. The small number of pathogens might be attributed to antibiotic treatment, but it is also possible that pneumonia and death were caused by the virus alone.

Our thanks are due to Dr. A. J. McCall and to Dr. E. M. Mackay-Scollay for their help and criticism, and to Dr. Peter Stock for clinical data.

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Infectious Diseases in England and Wales

Disease	Week ended November				
	2	9	16	23	30*
Diphtheria	5	4	5	4	5
Dysentery	282	216	278	433	461
Encephalitis:					
Infective	6	2	3	5	2
Post-infectious	3	3	4	17	—
Food-poisoning	174	126	136	243	151
Measles, excluding rubella	1736	1676	1697	1966	1843
Meningococcal infection	31	28	24	19	22
Ophthalmia neonatorum	22	29	28	26	36
Paratyphoid fever	8	5	15	4	5
Pneumonia, primary or influenzal	1443	742	623	499	486
Poliomyelitis:					
Paralytic	53	51	55	44	39
Non-paralytic	7	10	13	23	17
Puerperal pyrexia	285	261	220	217	208
Scarlet fever	444	444	550	612	772
Smallpox	—	—	—	—	—
Tuberculosis:					
Respiratory	541	543	505	585	595
Meninges and C.N.S.	6	4	7	3	9
Other	67	63	75	61	55
Typhoid fever	3	8	4	2	2
Whooping-cough	401	431	472	618	635

* Not including late returns.

In England Now

A Running Commentary by Peripatetic Correspondents

YESTERDAY the morning post brought an embarrassing revelation from my husband's past. It was an innocent looking letter from the M.R.C. and ran: "Dear Doctor: In 1951 you stated that you smoked an average of 3 cigarettes a day . . ."

Three cigarettes a day! When I met him, around that time, *thirty-three* a day would have been a conservative estimate. The mean has hovered around there ever since, plus or minus a few standard deviations. We sat dumbfounded, our bacon cooling unheeded. I broke the silence first. "Why you hypocritical old . . ."

Then I was aware that this was superfluous. My husband stared before him, automatically buttering toast.

"How could I," he began brokenly, "how could I say such a thing?"

But already it was obvious. My husband is a heavy smoker, except when Giving Up Smoking. This happens three or four times a year and lasts anywhere from half an hour to two horrible weeks. During these interludes he is very virtuous, impossible to live with, and, of course, convinced that smoke will never again pass his epiglottis. Clearly the questionnaire had caught him while he was Giving Up Smoking, or, more accurately, Tapering Off.

There it is: 3 cigarettes a day, all tabulated, analysed, with confidence limits and the rest of it. It makes you think. I mean, statistical methods are so reliable these days. Isn't it appalling that they have to depend on people?

* * *

As we say up here, there's guid gear in sma' bulk, and that seems to apply to salamanders as well as to *Homo sapiens*. Salamanders with big brain-cells can be produced by polyploidy—a kind of chromosomal polygamy. Triploid salamanders have an extra set of chromosomes, and brain-cells half as big again as normal.

But they are slow learners compared to their more modestly equipped brethren. Tetraploid salamanders have two extra sets of chromosomes and double the average size of brain-cell, and they are even slower learners than the triploids. According to the psychologists who carried out the experiment, what matters is not size but having the right connections—also a useful advantage in human affairs.

* * *

On the appointed day a ruffianly-looking gang assembled in the mine manager's office. We had been told to wear our oldest clothes and we looked more like an identity parade to pick out a gaggle of safe-breakers than a group of professional men.

We set off to the quartermaster to be fitted out with overalls and found that our assorted shapes and sizes took a bit of accommodating. When more or less overalled we were fitted with helmets and went to collect our lamps. The batteries were unhooked from the charging machine and fastened to our belts, a length of flex passing by way of a hook on the back of the helmet to the lamp clipped on the front. The switch gave a choice of two bulbs—side and head (or was it—dipped and undipped?).

After studying a map of the workings—and learning that we were going to be taken under the Irish Sea—we made for the pit-head, where we were frisked for combustibles and handed in the little metal tags which corresponded to our lamp numbers. We squeezed into a metal box and the door shut with a sinister clang—accompanied by the squeal of the doctor whose fingers had been gripping the bolt bar. We were off. A smooth acceleration—which was kinder to the liver than many a hotel lift—a few swallows to help the ear drums, and we were down.

We crawled out of the cage and made our way in single file along the rails. The crudely hacked walls and roof bore no resemblance to the Piccadilly line, and many of the horizontal pitprops showed greenstick fractures. Even the smallest of us had to walk in a crouching position with bent knees and a spine twisted to avoid the snags underfoot while at the same time keeping an eye to the assorted projections from the roof. There were few overhead lights and for much of the journey we depended on our headlamps. The ventilation system caused a not unpleasant breeze, but the rearward members of the party were engulfed in dust stirred up by our shuffling feet.

After about a mile we entered an airlock which admitted us to the workings. The closure of the airlock doors had gently assaulted our eardrums, but it seemed an immoderate door slam that greeted us as we emerged. We crouched against the walls while four more explosions greeted us. Shotfiring we were told. (The pit was a source of commercial quantities of methane, and our morale would have been improved if we had been told the significance of these explosions before they started.) We then moved forward to be met by a pleasant Guy-Fawkes-night smell and a cloud of coaldust. We had fondly imagined that the explosions were coming from a few hundred yards away and were surprised to find that thirty yards brought us to the coalface where men were already shovelling the coal dislodged by the shotfiring. They worked at great speed and soon the patient pit pony towed away eighteen hundredweight in a couple of tubs.

We moved to another cul-de-sac where they were using a deafening coalcutter worked by compressed air. This was a machine to cut horizontal clefts into the coal face to ensure that pieces of suitable size break away when the explosive charges are fired. One of our number pleaded claustrophobia and we started back. I asked our guide if roof falls were common. He said that there had been one that morning in the roadway by which we were now returning.

There was a long uphill walk back to the cage and the little headlamps got further and further apart. Our leader was in better training than we were and was twice seen to replace a loaded truck (eleven hundredweight) on the rails single-handed. Apparently the manager and his assistant spend nearly all their working time underground. This keeps them exercised and possibly contributes to the excellent working relationships at this colliery.

Back in the cage the door clanged shut to the accompaniment of unprofessional language (someone had been sitting on the locking bolt this time) and up we went. All our headlamp tags were claimed, and we showered, and rounded off our visit with an excellent cup of Coal Board tea. As I drank mine I pondered on conditions underground. I have seldom felt as conscious of the frailty of the human body.

* * *

Few men can enter their wives' baths without scalding; women can endure, or indeed enjoy, water temperatures consistently five degrees or more higher than the male can tolerate. At the same time, in spite of a generally more adequate panniculus adiposus, women seem hypersensitive to cold. The female range of working temperatures, in fact, is permanently set at a higher level. Is this a function of the X chromosome in the skin, or perhaps in peripheral heat-receptors? Or is the difference in the nerve-endings, that react contrastingly to œstrogen and androgen? Do women with virilising tumours complain that their usual baths have become too hot? Are spurious females with Turner's syndrome unable to share the bath water of their normal sisters? For the endocrinologist with plenty of bathrooms in his house, here is an opportunity for research.

* * *

She was a widow of eighty, but game. Her main complaint was not of her grossly œdematous legs but of the sad fact that no-one would employ her. She just couldn't manage on her pension, and, without work, how could she save enough for that coach-trip to Scotland on which she had set her heart? And would I tell her own doctor what medicine she needed, so as to save the expense of coming to hospital? Things had never been so black before and she didn't know what was to happen to her. . . . As our conversation proceeded, the embarrassing moment approached, as it has at every consultation for five years, when a brown-paper bag was shyly produced and pushed diffidently across the desk towards me. I have long since given up protesting at the handkerchief or packet of cigarettes it contains. But, on this occasion, I could not conceal my pleasure at the contents. With grave misgivings about her own means of support she was determined that mine should be more certain. The bag contained a pair of braces.

Letters to the Editor

A FUNCTIONAL NECESSITY

SIR,—It is useless to pretend that hospital staffing is without deficiencies and defects, but I find it difficult to believe that the creation of a new grade of subconsultant status, such as the "specialist" suggested in your leader of Nov. 30, is a solution to the problem.

From the outset of the Health Service the whole question has been bedevilled by the administrative necessity for defining grades (and with them their salary scales). This suggested "specialist" grade, which is intended to include practitioners who have completed their training and are awaiting a consultant vacancy, would embrace both senior hospital medical officers and time-expired senior registrars, and would be the normal stepping-stone to promotion. Presumably some fortunate men in training might skip this grade, but the majority would find it yet another hurdle. S.H.M.O.s have not been excluded from the ladder of promotion but they have assuredly found it devoid of rungs and it is difficult to believe that the new "specialist" would find it different.

It is well known that many S.H.M.O.s and senior registrars are now undertaking work that is strictly of consultant character. An investigation or survey of consultant and trainee establishment might well show a strange state of affairs. It should be recalled that such a survey was one of the key points in the Strachan report and has been regarded by the Central Consultants and Specialists Committee as an essential preliminary to any decision on the whole problem of hospital staffing. We do not know the full facts and figures and any views expressed elsewhere or here must suffer for that reason.

Your leader implies that representatives of the profession are opposed to a subconsultant or "specialist" grade and that is certainly the case. The reason lies in lack of confidence in the employing authorities who could abuse such a grade. Every citizen must approve of economy in national expenditure and it is reasonable to expect the State to try and obtain the best service at the lowest cost, particularly at the present time. The bitter experiences of the S.H.M.O.s is surely evidence of this. This grade was designed for restricted and limited purposes and it has always been hoped that it would diminish. The number of men in this "limited" grade is now 2600, over one-third of the consultant strength. The increase that has occurred has been outside the stream of general medicine and surgery where the appointment of S.H.M.O.s is prohibited.

Your leader aims at dealing with a problem that all agree is urgent, but is there not another more simple and equitable solution? If on a national survey it is shown that work of consultant character is being done by men who are not of this rank it is clear that there are further vacancies for consultants. It is not suggested that the new consultant appointed to such a post should necessarily expect all the advantages that were accorded to most consultants at the outset of the Service. He might well be expected to have charge of a limited number of beds, to undertake his own emergencies and the greater part of his operating work, and to have a smaller team. He would resemble the junior physician or surgeon in the "firm" system of the old voluntary hospitals and would in time have increased responsibilities, with more beds and a larger call on the services of junior staff. He would essentially be a consultant with the status and security of tenure that this grade implies and not a mere "specialist" who has yet to overcome another fence. A limited experimental venture of this order has already been successfully applied by the North West Metropolitan Regional Board a few years ago.

The merit of such a scheme would be that the fully trained practitioner would gain his consultant stripes nearer the age of 32 that was suggested in the Spens Report. He would no longer feel the frustration and delays that are inherent in the existing system, and which would be inevitable if a subconsultant grade were introduced. The cost to the State would only be the difference between the S.H.M.O. or top of the senior-registrar scale, and the basic salary for the consultant.

The whole problem has been obscured by terminology. All that we require is consultant status for men who are undertaking consultant work and responsibility, and as I have already said many S.H.M.O.s and senior registrars come within that category. If it can be shown that they are doing this work the vacancies exist. It is agreed that the consultant/trainee ratio is at present too high, but additional consultant appointments which do not require senior registrar or registrar assistance would help to improve the position, which at the moment is only being considered in terms of a "rundown" of trainee posts.

Any project to solve this problem should surely aim at upgrading if this is justified. Dilution or anything that gives the least opportunity for a substandard grade can only reflect badly on the Health Service as a whole. At the risk of repetition I ask whether the S.H.M.O.s and trained senior registrars, who would be embraced in this new grade, are satisfied with the way things have gone with them since the start of the Service and whether they would be happy to be placed in a subconsultant grade in the future.

There are many points in this disturbing problem that I have not touched on and as I have taken part in the discussion and negotiations since the inception of the Service I realise only too well the complexities and difficulties. Some of the problems may well be insoluble if they are to be fitted into a rigid administrative framework, but the facts must be obtained before any permanent solution can be attempted.

T. HOLMES SELLORS,
Chairman, Central Consultants and Specialists Committee.

PS.—The committee referred to in column 2 of your leader (p. 1099) should be the Joint Consultants' Committee, not the Joint Negotiating Committee. The latter was a body with different functions.

SIR,—You have referred to me in your leading article, and you will therefore doubtless let me comment upon this article, particularly as some of my views are not accurately represented.

You have again urged that a new grade "that of specialist" (as distinct from consultant) should be created in the hospital service in spite of my explaining that the profession has an agreement with the Minister that the word "specialist" shall never again be used owing to its dubiety and the impossibility of the public ever being able to discriminate between "consultant" and "specialist."

You state, quite wrongly, that I am unwilling to recognise such a rank as assistant physician and assistant surgeon. Why just put up illusory skittles for the sake of knocking them down? I am strongly in favour of assistant physicians and assistant surgeons—but employed on proper terms. This means assistant physicians and assistant surgeons as defined in the consultant Spens Report and as they exist, and have existed, for many years, in practically all our teaching hospitals. Such assistant physicians and surgeons are of full consultant status—i.e., employed on consultant terms—but occupy the junior position on a "firm" of two consultants. It is because regional hospital boards and hospital management committees have been defective in planning their staffs on these lines that much of our troubles are due and this should be rectified as soon as possible. I am not in favour of employing assistant physicians and surgeons on unfair, subconsultant terms.

Most senior registrars today have the training, qualifications, and skill of the young consultant of pre-Service days and are doing work that should be done only by

consultants. This is now, in addition, true even of a certain number of middle-grade registrars which makes the position still worse.

It is very easy for you to say in general terms that there is much work in hospital that consultants need not do. This requires, before it is a statement of any value at all, much more authoritative exposition of detail. Our chief concern is with the main clinical streams—acute medicine and surgery. This is where the staffing problems as well as other important issues affecting the future standards of medicine really lie. What work is there in these streams, to use your words, that "a consultant need not do" and that needs some subconsultant grade to do it? I can think of *none at all* but perhaps I say this with less authority than yourself to express an expert opinion. I can only claim to have been a consultant for 27 years, working daily in acute hospitals. Doubtless to think more soundly and authoritatively on clinical staffing problems I should have dropped all this many years ago, or never taken it up, but sat like Rodin's statue, pondering theoretically in an office. In other words, the answer to our staffing problems can come only from those who know from their own personal hospital and clinical experience just what those problems are.

Professor Strachan's committee, of whose report you make so much play, was appointed at my instigation when I was the chairman of the Central Consultants and Specialists Committee. The latter never approved of or adopted it and nor did the Joint Consultants Committee. Its great merit was that although it expressed various opinions with which there could not be agreement, it was provocative and stimulated fundamental thinking. It was passed on to the Ministry of Health for this stimulating effect (where it did not prove strong enough) and to start us talking but not as a set of ideas endorsed by the Joint Committee. Thus, neither the Central Consultants Committee nor the Joint Committee have had, as you suggest, "second thoughts."

Speaking personally, I have already said (and this is much on record) that staffing should be shaped to hospital needs and not for some advantage to staff, and you are in error in your article in suggesting that this motive has played any part in our professional policy. In acute medicine and surgery, if standards are not to fall, practically all the clinical work needs to be done by older or younger consultants with that degree of personal assistance (and no more than this) that they require from registrars and house-officers. If the Ministry and regional hospital boards had made this a strict criterion in planning then the supply of trainees would have been less than the demand and recruitment would be healthy because prospects would be good.

It is most important in replanning, or, rather, reforming our staffing, that the intermediate grades should be thinned out and not increased. Spens made a mistake with the grade of junior registrar and this post was eliminated some years ago. In my opinion experience shows that a mistake was also made over the senior registrar. He is really too senior and should be a young consultant at the beginning of his 10-year scale. We could do with a staffing structure in acute medicine and surgery of, say, 2 years' house appointments (including the preregistration year), then a maximum of 4 years as a registrar followed by the filling of consultant vacancies by competition at as early an age as possible. The net cost of this would be negligibly greater than the more complex and inefficient one of registrar, senior registrar, subconsultant, consultant. It is immensely important that the consultant age of appointment should not go on rising further towards middle life.

Here—in simple form—is the sort of action that should be taken now. There has been practically no increase in the number of general surgeons in the country since 1948 in spite of enormous waiting-lists, but the growth of senior registrars and registrars has been immense, a high proportion of them doing work that should be done by their chiefs. Let regional hospital boards promote at once to consultant rank in their present posts all those senior surgical registrars who are doing consultant work and who are suitably trained and qualified, with formal advertisement of the posts if this is considered necessary. Then the promoted men should not be replaced by further registrars.

In acute medicine and surgery the standards must remain wholly consultant for the acute hospital is the final court of clinical appeal. The acute hospital must never be the career refuge of the weak. It is wiser planning and not more money that is needed to bring this about.

There is a real danger today of a ruthless exploitation of our profession and a downgrading of the hospital service under narrow-minded and sometimes, I fear, not too scrupulous official pressure. We need to see this clearly and unmistakably and there must be no truck with a spirit of appeasement. I hope that *The Lancet*, with the speed of a blind Bannister in blinkers, will not lead us, with the best of intentions, in a rush downhill. What road is paved with such intentions? On the contrary, in these difficult uphill days, give us the example of being a stimulating Sisyphus for standards.

London, W.1. T. ROWLAND HILL.

SIR,—In your leading article you again campaign in favour of a subconsultant grade in the hospital service, and in this connection you quote various extracts from the report on hospital staffing compiled by the hospital staffing subcommittee of the Central Consultants and Specialists Committee of which I am chairman. You raise a number of points that could be discussed at length but I propose to confine myself to only one of these points.

It is fact that, with the object of avoiding large-scale unemployment within the ranks of the senior registrars, we did in that report recommend the institution of such a grade, but only along with efficient safeguards in order to prevent it from being used as a means of watering-down the numbers in the consultant grade. The most important of these safeguards was that an immediate review of hospital staffing should be carried out so that it could be ascertained in what hospitals and in which specialties posts of this grade should be instituted. Such a review would also let it be known to what degree, if any, the consultant establishment should be augmented.

When this report was passed to the Joint Consultants Committee, and when they discussed it with the Ministry, we found the greatest unwillingness on the part of the Ministry to institute such a review, and that state of affairs has persisted up to the present.

After making strong and repeated representations to the Ministry throughout a lengthy period without avail, we have lately ceased to support the idea of a subconsultant grade as, without the appropriate safeguards for which we asked, we consider that such a grade is bound to lead to the watering-down of the ranks of the consultants to their permanent detriment, while the quality of the hospital service would not be improved. This is the reason for our altered attitude to which you draw attention.

Our present position is that, before any other action is taken, a review of hospital staffing should be carried out, first locally and later at regional level, and that in the meantime time-expired senior registrars should be retained in their appointments with appropriate salary increments. Finally, throughout all our considerations we have held to one principle: that ultimate clinical responsibility for the treatment and care of patients must rest only with practitioners of consultant rank.

GILBERT I. STRACHAN,
Chairman of the Hospital Staffing Subcommittee of the Central Consultants' and Specialists' Committee.

Cardiff.

SIR,—I was glad to read your leading article. These facts have been very obvious to me for a number of years. I think it is useless approaching the Consultants' Committee on the matter, since I believe they feel it is not in their own interests to help, and therefore will show no sign of doing so. The only way to solve this problem is to approach the Minister of Health direct.

Aitken Sanatorium, near Bury, Lancs. F. R. GLOVER.

SIR,—In your leading article you again advocate the creation of a new "subconsultant grade" as a cure for the ills of the hospital service. Your reference to senior hospital medical officers must, however, surely have been made with your tongue in your cheek. Indeed, the history of this grade and the discontent that it has caused provides one of the most cogent arguments against your proposals. The S.H.M.O. grade was originally introduced as a temporary measure to cover those members of the hospital service whose qualifications did not measure up to the requirements of the consultant grade. Since then, however, the S.H.M.O. grade has been expanded out of all proportion and there can be no doubt that in many cases it is now being used as a source of cheap labour. In my own case, and in the case of many other S.H.M.O.s of my acquaintance, the work carried out is indistinguishable from that undertaken by consultants and consultant supervision is purely nominal.

You may attempt to sugar the pill by using such terms as "assistant physician" or "assistant surgeon", but these posts would not in fact be analogous to the junior posts of the pre-N.H.S. days. In those posts, the man appointed was a full member of the consultant staff of his hospital and was able to start building up his private practice. The attainment of consultant status in the N.H.S. should not be an indication of omniscience and this is surely implied by the salary structure with its incremental rises as the consultant becomes more experienced and by the system of merit awards for the more outstanding consultants. It should also be remembered that the levels of consultant remuneration were based on the assumption that training would be completed at about the age of 32 and if you now propose to institute an additional hurdle, the remuneration of the future consultant should in fairness be increased to compensate for the delay in achieving consultant status.

The underlying cause of the present crisis in the hospital service is the artificial restriction of the consultant establishment. There is little doubt that the proposed new subconsultant grade would be used as a source of cheap consultant labour and that in a very short time it would be a source of much frustration and discontent.

As a safeguard, therefore, before this new grade is considered further, the Ministry should be pressed to show its good faith by authorising the expansion of the consultant establishment to its proper level. After this has been done, the position could be reviewed to determine whether a new grade is still necessary for the *small number* of practitioners referred to in your extract from the Strachan report.

In the meantime, the position of senior registrars could be alleviated if they were to receive appropriate incremental rises in salary after their fourth year of service.

S.H.M.O.

SIR,—In your editorial you close with the words "it may first have to go back to the principles so clearly stated in the Strachan report." Your words are well chosen, for a more retrograde step it would be difficult to take. You are advocating that damning political move expediency is more important than principle.

If unhappily your words are heeded, in a few short years the appalling folly will become apparent, and you will be one of the architects.

Shenfield, Essex. W. DOUGLAS PARK.

SIR,—Your editorial makes interesting reading but scarcely touches the real troubles as registrars see them. Many, probably the majority, are in agreement in principle with a continuous grade embracing senior registrars and senior hospital medical officers, and (from the point of view of pay) overlapping, appreciably, the consultant range; but it is difficult to see how this alone will solve the problem or even work without changes elsewhere.

There is very deep and widespread distrust in the intentions of the Ministry and unfortunately, it must be said, of our own profession. Few can fail to be impressed by the palsied futility of the endless discussions and negotiations which have gone on since 1952 when the registrar position was made acute by the cut in senior-registrar establishments.

The domination of the whole hospital service by the teaching hospitals, which are in a minority (and a small one), the one-way traffic through these hospitals to most consultant posts, and the present methods of remuneration and organisation in general practice continue to be the main reasons why the present system of hospital staffing has failed and why your suggestions will be likely to fail too.

No registrar will agree to the introduction of a new grade or a continuous grade until many more consultant appointments have been made in the main specialties and the gross disparities of staffing which now exist rectified. He has put his trust in princes before.

Few appear to be aware how wide are these variations in staffing. I have numerous examples relating to general medicine and geriatrics but three will suffice.

I know of three areas where roughly equal populations are served, and where one consultant physician in each is responsible for 950, 500, and 250 "geriatric" beds. The ratio of "geriatric" to acute general medical beds in these three areas respectively is 6/1, 2/1, and 1/1. It was not until 1954, 1956, and 1957 respectively that consultants were appointed to these posts. Prior to this in the first and third a senior hospital medical officer was in charge in each, and in the second the 500 "geriatric" beds were served by two consultant physicians who already had 200 acute general medical beds between them.

A number of conclusions can be drawn from these figures, but it must not be forgotten that since 1952 large numbers of fully trained senior registrars in general medicine have been seeking desperately for permanent consultant posts, many being forced into other work or overseas, and that in the middle of 1955 there were 770 unfilled "junior" hospital posts in England, Wales and Scotland.[1]

I wonder how one can start to assess equitable rates of pay for hospital staff when such gross disparities exist.

Harrow Weald. F. ALLEN BINKS.

SIR,—Your further article on the question of hospital staffing is very welcome, as we cannot afford to ignore this difficult problem indefinitely. I believe your solution, the "functional necessity" of a new grade of assistant consultant, is the right answer.

The "career grade" or "senior hospital officer" of the Strachan Report was widely criticised in that it appeared to be a kind of dead-end post, encouraging mediocrity, and perpetuating a "stooge grade" of subconsultant. Many of us voted against it on these grounds in our local discussions at the time of the report; and most of the criticisms of the suggestions in your June article[2] were on the same lines.

My excuse for writing again on this subject is my wish to emphasise what I believe to be the fundamental point of my original letter[3]: that the appointment of an

1. Report of the Committee to Consider the Future Numbers of Medical Practitioners and the Appropriate Intake of Medical Students. H.M. Stationery Office, 1957.
2. *Lancet*, 1957, i, 1127.
3. *Ibid.* Aug. 3, 1957, p. 240.

assistant surgeon or physician would be regarded as an appointment to the hospital consultant staff; and that promotion to full consultant status would be as automatic as was the case before the war. This expectation of promotion would remove at once the fears of a permanent "subconsultant grade," and the lack of security which so bedevils the outlook of our senior registrars. I envisage the appointment of an assistant consultant in most of the non-teaching hospitals where there is at present a senior registrar. The work of the assistant consultant would be much the same as that at present done by the senior registrars, with a limited number of beds and a salary similar to that of a first-year consultant.

Junior hospital staffing would need some adjustment; senior registrars might well be restricted to teaching hospitals; and other registrars work only in non-teaching hospitals (as suggested at a recent meeting in Birmingham).

Three decisions seem to be required:

(1) That something must be done, and done soon. It is no longer fair to expect a man of senior-registrar standard to spend four vital years in a peripheral hospital with such poor prospects of a consultant post as are now available; and whether we care for justice or not, the men will not be forthcoming; already the standard of applicant for such posts has fallen considerably.

(2) A decision as to what should be done. From conversations and "personal communication," I am convinced there is widespread support for some change of this kind. A nationwide review of the question as was made at the time of the Strachan Report might reveal a strength of opinion sufficient to persuade Mr. Holmes Sellors and Professor Strachan to unbend a little from their "whole consultants and nothing but consultants" attitude.

Dr. Rowland Hill fundamentally agrees with the principle in his advocacy of the "medical or surgical unit" with the junior member of the team sparing his senior from some of the routine work. The financial implications of the scheme are, of course, serious at this time of economic stress, but I believe the cost would be less than half of Dr. Hill's estimate of £2,000,000 per year.

(3) A decision as to how to persuade the Ministry to implement whatever schemes were generally approved. As you say, Sir, this profession should give a lead and in this case the profession means the consultants and the Royal Colleges. We are at present wide open to the charge of complacency, indifference, and the "pull-up-the-ladder-Jack" attitude; while the cloud is already visible in the sky, presaging a storm which may rock and eventually even wreck the boat.

Somehow the Joint Negotiating Committee must be empowered to press most strongly for action, and it is up to us to give them this power.

Coventry. T. H. BERRILL.

*** We are glad to have these clarifying letters.

Dr. Rowland Hill asks us to give examples, from "acute medicine and surgery", of specialised work which need not be done by a consultant. In our opinion a modern hospital department should always have someone on the spot to deal with such rapidly changing situations as the shift of electrolyte balances in patients with vomiting or diarrhœa, the response of infections to treatment, and alterations in prothrombin-time during anticoagulant therapy. Surgical practice includes much work that requires skill rather than judgment—*e.g.*, plaster work and manipulation in orthopædics, cutting grafts and raising pedicles in plastic surgery, and some routine operations in general surgery. All these things can be done by registrars. Our point was that already, in the peripheral hospitals, there are not enough registrars to do them. Who is to take their place?

We agree that many S.H.M.O.s are doing consultant work; but their grade has usually been decided by professional committees—anxious, like Dr. Rowland Hill, to maintain standards. S.H.M.O. posts are created in accordance with a formula to which the profession's representatives agreed (R.H.B. [50] 96); and the increase in their number, which Mr. Holmes Sellors deplores, can be regarded as good evidence that an intermediate grade is really needed.

The agreement so urgently necessary is hindered by terminology. Our proposal is simple—namely, that the person who has been trained in a specialty goes into the administrative grade of specialist, and is called assistant physician, assistant surgeon, assistant pathologist, assistant radiologist, according to the post he occupies. For those who do not later get consultant appointments the specialist grade should offer permanently satisfactory conditions, including a salary for its senior members well above that of newly made consultants. In one sense we are creating a new grade, but in so doing we get rid of an old one—that of S.H.M.O.—which has always been bad because it was a step off the ladder of normal promotion.

In their plans for the future consultant, our correspondents seem to us to pay too little attention to the S.H.M.O. Because they think that a non-consultant specialist ought not to exist, they tend to forget that he does and must.—ED. L.

FULMINATING ABACTERIAL INFLUENZA

SIR,—We should like to remind readers that death may occur from the effects of influenza virus alone, in the absence of any bacterial or other significant complicating factor.[1] This is not to contest the substance of your leading article of Oct. 26 nor of the several recent contributions, notably those of Dr. Gunn (Nov. 16) and Dr. Roberts (Nov. 9).

Since the epidemic of 1919 it has been maintained that death from influenza means death from lung complications—pneumonia in some form. This type of statement is to be found in many textbooks, and the assumption that bacteria alone are responsible has led, we believe, to the ignoring of the effects of viral invasion and of the reaction of the tissues to this invasion. Dr. Roberts alone has recently mentioned that it would be unwise to dismiss the possible toxic effects of a massive virus infection.

Our own evidence is based upon the post-mortem examination of three children, aged 3, 9, and 11 years, who died during the recent epidemic.

A 3-year-old boy, who suffered from infantile eczema and asthma, died an asphyxial death after mild upper respiratory symptoms lasting less than 24 hours.

A 9-year-old girl was a known diabetic. She had been drowsy for 3 days, with some vomiting. On admission to hospital the blood-sugar level was 500 mg. per 100 ml., and, after a few hours of fluid and insulin therapy given under strict biochemical control, and when the child had recovered sufficiently to sit up and talk, she died an acute asphyxial death. Retrospective inquiries revealed the presence of other cases of influenza in the home.

An 11-year-old girl died a few hours after having been passed by her general practitioner as suffering from typical and mild influenza. The duration of her illness did not exceed 48 hours. She was the only one to receive any antibiotic—penicillin by mouth 6 hours before death.

Influenza-A virus (Asian type) was isolated from the lung of this last case; attempts to isolate virus from the first were unsuccessful, perhaps because of the time which elapsed (24–30 hours) between death and necropsy.

In none of the cases were any recognised pathogenic bacteria isolated from the lungs or trachea, though *Staphylococcus pyogenes*, *Hæmophilus influenzæ*, and hæmolytic streptococci were specifically looked for.

The striking feature at each necropsy was the presence of a fine tenacious froth which filled the air passages from the small bronchi even to the lips, a froth which was quite indistinguishable from that seen in cases of drowning. Struck by the similarity to the appearances in drowning, we analysed the fluid from two of the cases

1. Hess, J. F. P., Mulder, J. *J. Path. Bact.* 1957, **73**, 565.

and found their protein contents to be 5·8 and 7 g. per 100 ml. That they were composed of normal serum was confirmed by paper electrophoresis.

The histological examination of the lungs, which will be reported in more detail later, shows a distinctive though patchy pathological process. The earliest lesion is probably a swelling of the alveolar epithelium whose cells, normally flattened, become distended and cuboidal, and the septa avascular. This probably progresses to a frank ballooning of the cells, to some desquamation and autolysis. The alveolar spaces become plugged with serofibrinous fluid in which only the ghost-like outlines of septa remain. The trachea in one case shows loss of mucosa, but the small bronchi little change.

Most histological accounts of influenza, whether natural or experimental, have suggested that the earliest changes, and the earliest localisation of virus as shown by fluorescin-labelled antibody, have always been in the mucosa of the turbinates and of the trachea.[2–4] Specific alveolar changes due solely to virus do not appear to be well recognised. Our findings closely resemble those reported by Tyrell and Cameron [5] as occurring in the lungs of suckling mice infected with influenza virus, and we feel that they are probably specific, at least for the prevalent strain of influenza virus.

That death may occur from influenza is readily explicable from the pathological findings. The flooding of the alveoli with pure serum, whilst providing an ideal culture medium for any pathogenic bacteria, is at the same time sufficient to produce an asphyxial state.

We conclude that death may occur before any secondary invasion takes place. Furthermore, this death appears to be due to viral invasion, or perhaps more specifically to the reaction of the tissues to that invasion. This would support Dr. Breen's suggestion (Nov. 16) that it is not the invading organism which kills, but the patient's overemphatic reaction to it, and the young mean age of most fatal cases might further support this thesis.

Any rational therapy, and cortisone would seem to be highly rational, must be directed towards preventing such an outflow across the damaged alveolar walls.

Group Pathological Laboratory, Warwick.

D. F. BARROWCLIFF
A. P. PRIOR.

IMPORTANCE OF THE ILEUM IN THE ABSORPTION OF VITAMIN B_{12}

SIR,—Recent correspondence has shown differing opinions concerning the site of absorption of vitamin B_{12}. Dr. Doig and Dr. Girdwood (Nov. 23), from experiments on rats, concluded that it was absorbed from any part of the intestine, while Dr. Mollin and Dr. Booth (Nov. 16 and 30), utilising observations on human subjects in addition, favour the site of absorption in the ileum. McIntyre et al.[6] studied two patients who had resections of all the small intestine save about one foot of jejunum and found that the absorption of radioactive B_{12} was negligible in both. Kogan et al.[7] and we ourselves have each made like observations on similar patients. McIntyre et al. also demonstrated impaired absorption in 3 other patients with regional ileitis, 1 of whom had only the terminal two feet involved. They concluded that the major site of B_{12} absorption may be in the lower small intestine. Our experiences have been similar, for in 9 patients in which the lesion has been confined to the ileum (in 6 the lesion had been resected), vitamin-B_{12} absorption was impaired in all (fæcal excretion of 0·5 mg. B_{12} ^{58}Co range 65–91%). 2 further patients, however, who had the disease limited to the duodenum and jejunum had normal B_{12} absorption (fæcal excretion B_{12} ^{58}Co 45% and 32%). The second of these patients, moreover, had had a resection of three feet of his jejunum.

We have called attention [8] to the high incidence of vitamin-B_{12} deficiency in regional ileitis and in a more recent survey of 70 patients, 60% were found to be deficient. We are in no position to express views on the site of absorption of vitamin B_{12} in the intestine of animals but as far as man is concerned, the evidence does appear strong that the major site of absorption of the vitamin is the lower ileum. If vitamin B_{12} is absorbed from the jejunum it can only be in small amounts of no great practical significance.

The General Hospital, Birmingham.

W. TREVOR COOKE
E. V. COX
M. J. MEYNELL
R. GADDIE.

SIR,—It is encouraging to note that Dr. Booth and Dr. Mollin (Nov. 16 and Nov. 30) have so amply confirmed our original observations with normal rats.[9] Although our results would indicate the possibility of absorption occurring in less than 1 hour we must conclude that our interpretations are now essentially the same. It would appear that the main absorption of the vitamin does occur in the mid-segments of the small intestine.

Department of Pathology, Royal Victoria Infirmary, Newcastle upon Tyne.

A. L. LATNER
LAUREEN RAINE.

LEAD POISONING

SIR,—Dr. Davidson, in his article of Nov. 30, accepts almost by implication that the route of absorption of the lead from the remnants of broken-down car batteries was inhalation.

In the Rotherham outbreak, on which you published my findings,[10] I postulated the theory that the absorption of lead from a similar source was due to ingestion and suggested that the careless food hygiene of the affected children was responsible for this. I wonder whether Dr. Davidson has any evidence that this was the route of entry in his cases.

Civic Centre, Dagenham.

J. ADRIAN GILLET.

ROAD-MENDING AND CLEAN AIR

SIR,—We have read with interest and some concern the comments appearing in your annotation (Nov. 23). We can appreciate the importance of these views and what has prompted them, but it would appear that they are naturally of a general nature and do not take into account modern developments.

In the first place there has been a rapid change in the mixers and other types of plant employed in road-surfacing work whereby solid fuel has been replaced by oil-burning, with consequent advantages in the absence of smoke.

We feel, moreover, that the remarks apply particularly to the removal of surface treatments, and not to the actual road-laying operations with asphalt materials, as is suggested. In this connection, however, it must be appreciated that the proper heating and removal in maintenance work of asphaltic materials need not, and does not, necessarily produce much smoke, but certain types of road dressings when removed by the same heat treatment can be a hazard. It is satisfactory to report, however, that there is a proprietary material, which is being extended in its use, which is designed to do this very thing that seems so desirable—that is, to eliminate the smoke

2. Straub, M., Mulder, J. *ibid.* 1948, **60**, 429.
3. Mulder, J., Verdonk, G. J. *ibid.* 1949, **61**, 55.
4. Liu, C. *J. exp. Med.* 1955, **101**, 665.
5. Tyrell, D. A. J., Cameron, A. H. *J. Path. Bact.* 1957, **74**, 37.
6. McIntyre, P. A., Sachs, M. V., Krevans, J. R., Conley, C. L. *Arch. intern. Med.* 1956, **98**, 541.
7. Kogan, E., Schapira, A., Janowitz, H. D., Adlersberg, D. *J. Mt Sinai Hosp.* May 1957.
8. Meynell, M. J., Cooke, W. T., Cox, E. V., Gaddie, R. *Lancet* 1957, **i**, 901.
9. Latner, A. L., Raine, L. (1957). Vitamin B_{12} und Intrinsic Factor. 1. Europäisches Symposion Hamburg 1956, p. 243. F. Enke, Stuttgart.
10. *Lancet*, 1955, **i**, 1118.

normally engendered by these heat treatments, and this would appear to answer the recommendation made in your concluding paragraph.

A. W. ATTWOOLL,
Executive technical director.
Limmer and Trinidad Lake Asphalt Co. Ltd.
London, S.W.1.

ATARALGESIA

SIR,—The article by Dr. Hayward-Butt in your issue of Nov. 16 will be of considerable interest to all anæsthetists, particularly to those who are attracted by the problems of obstetric anæsthesia.

It is evident that there is in many places a groping towards a new form of pain relief in operative obstetrics.

Davies [1] referred to five cases of cæsarean section in which 25 mg. of chlorpromazine was given intravenously 30–45 minutes before operation, anæsthesia being induced and maintained with a nitrous-oxide/oxygen mixture, plus succinylcholine when relaxation was required.

More recently, Scott and Gadd [2] suggested that a number of forceps deliveries could be satisfactorily undertaken following the intravenous injection of 100 mg. pethidine and 25 mg. chlorpromazine.

Dr. R. E. Molloy, who arrived at this hospital a couple of months ago, informs me that when he left the Whittington Hospital a substantial number of cases had been conducted there in this manner, with fully satisfactory results. I have commented upon this trend in a general review shortly to be published,[3] and have referred also to a number of forceps deliveries which, in cooperation with Mr. J. D. O'Sullivan at St. Mary's Hospital, Portsmouth, I conducted satisfactorily with 150 mg. pethidine and 50 mg. chlorpromazine given intravenously. Although this series was prematurely concluded, owing firstly to intervening vacations, and then to my leaving for Pittsburgh, it was obvious to us that the method had considerable potential value, though modifications would be advisable.

Evidently Dr. Hayward-Butt is also engaged in this movement. He mentions that he has given his "unit mixture" (number of units unspecified) in four cases of cæsarean section (three times intramuscularly, once intravenously). One would like to know in more detail the exact dosage given, the length of time between administration and the delivery of the child, and the precise condition of all the neonates. We still know too little about the placental transmission of the drugs in question to be able to ignore these details. I used chlorpromazine in my cases, but it might well be that in a larger series the sympathicolytic and other effects mentioned by Dr. Hayward-Butt (though not recorded in my patients) might encourage the use of 'Pacatal' in its place. If an opiate antagonist is to be used (and again I must quote the fact that in my own cases and those seen by Dr. Molloy there was apparently no pressing need for one, judging by neonatal depression, though the results would probably have been even more impressive had such an antagonist been incorporated in the mixture) I would suggest that levallorphan, rather than amiphenazole, be chosen. Levallorphan is apparently almost specific against narcotics, and is virtually innocuous both locally and generally, even when given in high doses intravenously—as is well recognised in this unit.[4]

Despite Dr. Hayward-Butt's preference for intramuscular injection, on the ground that it leads to less mental clouding, I would favour the intravenous route as there must be a more precise prediction of onset of effect, and in emergency cases (such as obstetrics) a 30-minute delay would be contraindicated.

I earlier used the term "conducted" because I am not happy about the question of nomenclature. Dr. Hayward-Butt uses the word "ataralgesia" to describe the state of each of his patients. Mine, however, certainly had some "disturbance of mind": I could converse easily with some, but others appeared to be in a semidrunken state, and a high proportion had amnesia for some of the events of delivery, though none recollected feeling pain. I had, perhaps clumsily, dubbed this state as one of "hypoæsthesia," in an attempt to indicate a diminution of awareness without loss of consciousness. As must be obvious, I have no Greek.

A further point which interests me, and one which will perhaps be the most intriguing to all anæsthetists, is how Dr. Hayward-Butt conducted the five abdominal operations for which no anæsthetic was given. If no relaxant drug was used, then this would imply a most interesting supplement to our knowledge of the pharmacology of pethidine and pacatal. If relaxants were employed, were the patients intubated, was their respiration assisted or controlled, and did they accept such manœuvres with ataralgesic tranquillity?

Mercy Hospital,
Pittsburgh, Pennsylvania. J. SELWYN CRAWFORD.

1. Davies, J. I. *Canad. Anaesth. Soc. J.* 1955, **2**, 327.
2. Scott, J. S., Gadd, R. L. *Brit. med. J.* 1957, **1**, 971.
3. Crawford, J. S. *Brit. med. Bull.* (in the press).
4. Foldes, F. F., Lipschitz, E., Weber, G. M., Swerdlow, M., Pirk, L. A. *J. Amer. med. Ass.* 1956, **160**, 168.

CORONARY AND AORTIC ATHEROSCLEROSIS

SIR,—Dr. Elkeles' report (Oct. 12) on the greater prevalence of aortic calcification in older women as compared with men, in contrast to coronary-artery disease, is in good agreement with our findings, not quoted by him, first published in 1954 [1] and subsequently amplified.[2 3]

Our actual prevalence-rates for these shadows at various ages were within the general range reported by Dr. Elkeles, and our diagnostic criteria, verified by comparing pre-mortem radiographic findings with post-mortem specimens from the same individuals,[4] appear to be similar. We felt rather humble when we found that Rokitansky already knew of the greater prevalence of aortic atheromata in women.[1 5] Subsequently, Barr, in an extensive review,[6] referred to an even earlier report by Hasse.[7]

Since you have lately given much space to atherosclerosis, I am taking the liberty of drawing your attention to an extensive epidemiological study of atherosclerosis from which these data have been taken. We have studied about 1200 men and women aged 40 and over, chosen strictly at random from a population of about 33,000 employed clothing workers in New York City.[2 3] Most were of Italian or Jewish extraction and were closely comparable from a social, economic, and occupational point of view. Our data are among the very few currently available,[8] relating to the prevalence of manifest atherosclerosis and associated factors in representative samples of population segments. Since most of Dr. J. N. Morris' extensive data on ischæmic heart-disease in various occupational groups in Britain are based on incidence- rather than prevalence-rates, a comparison with our data cannot be readily made.

Among the Italian-American men in our group, the prevalence of manifest coronary-artery disease, diagnosed on the basis of a history of an acute heart attack, unequivocal angina pectoris, or clear electrocardiographic findings, was about the same as for the other groups studied in the United States.[8]

In the Jewish men, on the other hand, the prevalence-rate was twice as high ($P < 0.01$). No ethnic difference in the prevalence of coronary-artery disease could be detected among the women. These findings were confirmed by analysis of certain insurance records, as we have reported. Radiological evidence of calcification in the thoracic and abdominal aorta likewise

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2. Epstein, F. H., Boas, E. P., Simpson, R. *J. J. chron. Dis.* 1957, **5**, 300.
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4. Hyman, J. B., Epstein, F. H. *Amer. Heart J.* 1954, **48**, 540.
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6. Barr, D. P. *J. chron. Dis.* 1955, **1**, 63.
7. Hasse, K. Krankheiten der Zirkulations- und Respirationsorgane. Leipzig, 1841.
8. Measuring the Risk of Coronary Heart Disease in Adult Population Groups; a Symposium. *Amer. J. publ. Hlth*, suppl. April, 1957.

was not different in the ethnic groups, again pointing to dissimilarities between coronary-artery and aortic disease, as discussed by Dr. Elkeles. On the other hand, coronary-artery disease appeared to be more common among the men with aortic calcifications than among those without such lesions; these particular data were insufficient for statistical analysis.

Thus, some degree of association between these two lesions may exist. In this connection, the inadequacy of available methods for the clinical diagnosis of both coronary and aortic disease cannot be overstressed. With Dr. Elkeles' and our data as a base-line, it might be of interest to determine the prevalence of radiologically demonstrable aortic calcifications in older people belonging to populations said to be relatively immune to atherosclerosis; the possible radiological hazard must, however, be kept in mind.

On attempting to explain the greater prevalence of coronary-artery disease among the Jewish men, we found that the dietary patterns of these particular Italian and Jewish groups could not provide more than, perhaps, a very minor clue; caloric and total fat intake was closely similar in the two groups even though the Jews, on an average, consumed about 10 g. more animal fat a day than the Italians, in isocaloric exchange for fat of vegetable origin.[9 10] Unfortunately, we could not compare the diets of the men with and without coronary-artery disease, since the number of diseased individuals was too small for valid analysis—a frequent consequence of working with random populations rather than sick persons and "controls". On further analysis, we were surprised to find that elevation of serum-cholesterol, blood-pressure, and weight was associated with a greater frequency of coronary-artery disease only among the Italian men; none of these three factors, alone or in combination, appreciably affected the disease-rate in the Jewish men. The conclusion appeared inevitable that factors other than those investigated in this study predisposed these Jewish men to the development of coronary-artery disease.

These data are somewhat at variance with recent reports on Jewish groups in Israel.[11 12] Space does not permit discussion of possible reasons for this divergence; but, as Sir Sheldon Dudley pointed out, epidemics of the same disease may be caused by dissimilar combinations of factors, according to time and place.[13] He referred to transmissible diseases, but his point applies equally to the epidemiology of non-infectious conditions. It goes without saying that we have talked of "Italians" and "Jews," but refer only to the particular Italian and Jewish Americans in our study. The epidemiology of atherosclerosis no doubt differs among people in these broad groups according to their given ecological setting. Nor do we wish to imply that our findings necessarily suggest that a genetic factor is involved in the observed differences, since there are many environmental variables of possible significance that were not studied in our investigations. We all hope that atherosclerosis and coronary-artery disease will eventually turn out to be largely due to things we do rather than to what we are. Our study is relevant—not so much, perhaps, because it constitutes a small link in the growing chain of epidemiological knowledge of these disorders, but because it demonstrates that such studies, involving statistically valid population samples and the simultaneous testing of multiple variables, are feasible and accurate within the limitations of currently available methods.

FREDERICK H. EPSTEIN.

Department of Epidemiology,
University of Michigan School of Public Health,
Ann Arbor, Michigan, U.S.A.

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TIME AND THE NURSE

SIR,—How I agree with points raised in your annotation of Nov. 30, particularly the reference to routine temperature recording.

In most cases, pyrexia has subsided within forty-eight hours nowadays and four-hourly temperature charts are a waste of time and paper, with a few obvious exceptions. Often as a busy night-nurse have I cursed the day-sister who demanded four-hourly temperature recordings on as many as 20 out of 30 medical patients, most of whom were admitted for investigation only.

Now as a ward-sister myself, I only wish that student nurses showed the same competence in the use of the sphygmomanometer, when occasion demands, as they do in the use of the thermometer.

I also suspect that many housemen and registrars, already indoctrinated into the orthodox methods, would recoil with horror at the thought of a blank temperature chart for any patient.

Regular temperature recording is just one of many hospital rituals, which also include daily weighing of healthy infants, waking patients at the crack of dawn, and polishing ward floors to mirror-like smoothness.

These customs are handed down to us with our black stockings and "dog collars" as a relic of the Victorian era. We can dispense with much of this and yet maintain our standard of bedside nursing.

Discretion compels me to remain anonymous, lest genteel cries of "Mutiny!" rain down upon my head from members of the nursing hierarchy.

MUTINEER.

PNEUMOCONIOTIC NEUROSIS

SIR,—It is axiomatic that before change is thought necessary in an existing procedure, one should prove beyond reasonable doubt that it is ineffective; it is always advisable to back reforming zeal with a few practical suggestions as to what changes are necessary and why. I submit that Dr. Macdonald (Nov. 23) has not even begun to prove his case; if he will look back through the correspondence on this subject he will see that I never asserted that "all was well" in regard to pneumoconiosis assessment. It is indeed fairly obvious from the letters of Dr. Dünner and Dr. Hardy (Nov. 23) that there are discrepancies between the standard of assessment of pneumoconiosis boards throughout the country; according to them some boards appear to be human enough to make an assessment against the radiographic evidence—which at any rate attests to their pursuit of fairness if to nothing else.

Meanwhile, Dr. Macdonald thumps the tub of destructive criticism and assures us that better things happen in South Africa, where geographical and climatic conditions are different. Great attention has been given by correspondents to the "initial radiograph," which seems to have been seized upon as the sinister motif to the whole situation. It is only an initial measure done to prevent bias, since any doctor, even a member of a pneumoconiosis panel when acting outside his official capacity, can examine a patient and certify that he has pneomoconiosis on a chit to the local Ministry of Pensions, thus initiating normal procedure. This rather clumsy method of ensuring fairness seems to have given rise to serious misunderstanding. There are in addition four radiographic stages of the disease upon which, together with clinical examination, exercise-tolerance test, &c., compensation is finally based. But the very point I have tried to make is that these radiographs are no more responsible than any other part of the examination for the ultimate assessment.

I will not endeavour to refute Dr. Dünner and Dr. Hardy's assertion that the decisions of boards are based on the "strict legal definitions of pneumoconiosis within a general legal directive". According to my information the boards are solely responsible for the diagnosis and disablement question. There is, of course, a prescribed list of dusty occupations together with a thoroughly badly worded pamphlet, *Medical Notes on Pneumoconiosis*, issued in 1951 by the Ministry of National

Insurance, which I sincerely hope boards do not follow to the letter.

Your correspondents wish to make bronchitis and emphysema a compensatable industrial hazard of working in dusty occupations. It has been shown in what little research has been done on this problem that town-dwellers generally begin to suffer from chronic bronchitis between the ages of 40 and 50 and breathlessness as a result appears in the next decade, presumably owing to the resultant emphysema. I submit that emphysema is a common autopsy finding in industrial cities in patients who have died at an advanced age; and beyond vaguely inferring the fact that those exposed in dusty occupations may be more prone to chronic bronchitis than others in cleaner trades, one cannot prove anything on this subject from postmortem findings, since the cause of death is usually some other terminal catastrophe. At all events your correspondents' series of cases appear to be incomplete and they appear to ignore any predisposition due to whooping-cough or other previous pulmonary infection.

How do your correspondents propose to detect emphysema caused by dust if it cannot be shown radiographically? Suspects can be given repeated clinical examinations for a lengthy period of time whilst in a dusty occupation, but the results of this are if anything more open to human error and misinterpretation than the radiograph showing the dust which accompanies the emphysema. How would one discriminate between this emphysema and that caused through excessive smoking or bad domiciliary ventilation or previous disease? The question is made all the more confused because we are here dealing with a series of symptoms which finally lead to a condition which disables only at the latter end of life. We have as yet only touched by research on the causation of bronchitis and its sequalæ by the impurities in the air of our industrial cities; and until much more is known about this I submit we cannot view the question of emphysema as an industrial hazard in its proper perspective. It would be interesting to know how the South Africans have tackled this problem.

Barnsley. J. D. M. HOLT.

EARLY ADMISSION TO HOSPITAL OF MENTALLY DEFECTIVE BABIES

SIR,—The parents of mental defectives will be grateful to Dr. Leys (Nov. 23) for the sympathetic attitude he shows towards their problems, and in return, I am sure, will be glad to supply him with the information he desires [" we badly need to learn from parents themselves, in situations which allow them to be truthful, what their needs really are "]. If he will get in touch with the National Society for Mentally Handicapped Children, 162a, Strand, W.C.2 (with a membership of 14,000 parents of such children) I think he will find what he desires.

London, N.W.11. E. HINDEN.

Parliament

Hospital Building

In a written answer on Dec. 6 Mr. DEREK WALKER-SMITH, the Minister of Health, announced that it was proposed to spend £22 million on capital development in the hospital service in England and Wales in 1959–60, compared with £18 million this year and £20 million proposed for next year.

Hospital boards were being informed of their individual allocations within this total for the modernisation of mental hospitals, the replacement of obsolete plant, and ordinary capital expenditure. In addition, the programme of major building projects would be continued and extended. As a former Minister explained in July 1955, the original programme, in order to encourage speedy action, included more projects than it would be possible to start in the years to which it was allocated. Projects already in the programme, but not started, and the second phases of some of those for which only the first phases had so far been authorised, were likely to make a considerable claim on the capital available for 1959–60. Mr. Walker-Smith had invited boards to bring to completion the planning of a number of additional major projects. He hoped that all boards would endeavour to complete the planning early in 1959–60.

The projects selected included the first phases of new hospitals to be built at Liverpool and Boston, and the second phases of a number of large schemes already in the programme such as the new hospitals at Huddersfield, Swansea and Swindon; the mental deficiency hospital at Llanfrechfa Grange, near Newport; the development of The Downs Hospital, Sutton, as a medical nuclear physics centre; and the provision of a new X-ray department and theatres at Lewisham Hospital where the first stage of development was now nearing completion. There were new outpatient departments for the Dudley Road Hospital at Birmingham, the Chester Royal Infirmary, and the North Staffordshire Royal Infirmary, Stoke-on-Trent; an outpatient department and admission unit to serve the Hollymoor and Rubery Hill Mental Hospitals; and an admission unit and convalescent villas at the Garlands Mental Hospital, Carlisle.

A new regional neurosurgical unit was included for the Newcastle General Hospital. Extensions were proposed at the Pontefract General Infirmary, Sharoe Green Hospital at Preston, the Blackpool Victoria Hospital, Blackburn Royal Infirmary, and Bronglaise Hospital, Aberystwyth; and works of modernisation were included for St. James's Hospital, King's Lynn; the City Hospital, Exeter; St. Lawrence's Mental Hospital, Bodmin; and Hope Hospital, Salford. Among the projects were a new boiler-house for the Manchester Royal Infirmary and some improvements at the City General Hospital, Sheffield. He was also asking for plans to be prepared for the first phase of some hospital development in Hull, and for additional beds at Ilford or Barking, but details of these two schemes had yet to be worked out with the boards concerned.

First Reactions to the Wolfenden Report

IN the course of a debate in the House of Lords on Dec. 4 Viscount KILMUIR, the Lord Chancellor, indicated the Government's preliminary views on the report. The most far-reaching of the proposals, he said, was, of course, that homosexual behaviour between consenting adults should no longer be a criminal offence. Though the recommendations had attracted considerable support, including some in informed and responsible quarters, it had also been widely criticised, and again some of the criticisms had been well-informed and responsible. There were cases Lord Kilmuir agreed when it might well be the duty of a Government to lead rather than to follow public opinion, but in a matter of this kind the general sense of the community was important, and the Government did not think that it was with the Committee in this recommendation. They thought that the problem required further study and consideration. Certainly there could be no prospect of early legislation.

One of the Committee's most important recommendations in Lord Kilmuir's view was that relating to research. So much had been written and so little was really known about the nature and origins of homosexuality, and also of prostitution, that further research was clearly desirable, and he assured Noble Lords that the Government would give attentive thought to this recommendation which had repercussions far beyond the sphere of criminal law.

Opticians Bill

Mr. RONALD RUSSELL, in introducing the second reading of this Bill on Dec. 6, said that since it was published he and his co-sponsors had met representatives of ophthalmologists and of dispensing opticians and after discussion of their criticisms [1] had agreed to amend the Bill in some respects if it went to committee.

Mr. RICHARD THOMPSON, the parliamentary secretary to the Ministry of Health, said that the Bill followed closely most of the recommendations of the Crook report. The suggestion that the Bill would interfere with the present common practice whereby an ophthalmic medical

1. See *Lancet*, Dec. 7, 1957, p. 1166.

practitioner tested sight on the premises of a firm of dispensing opticians was based on a misconception. If it seemed appropriate that a clarifying amendment putting the issue beyond a peradventure should be made in committee, it would certainly have the wholehearted support of the Government. The many points of detail in this Bill were, he was sure, capable of being resolved in committee without too much difficulty, and subject to such improvements, the Government welcomed the Bill.

Divorce for Insanity

On Dec. 6 Mr. W. F. DEEDES moved the second reading of his measure, the Divorce (Insanity and Desertion) Bill, which removes some small anomalies in the present law to which the recent Royal Commission drew attention. The most important amendment is to recognise treatment as a voluntary patient as a ground for divorce for insanity. At present divorce is only available to the spouse of a certified patient. It also proposes that a break of 28 days or less should not be regarded as interrupting a continuous period of care and treatment, and that desertion need not necessarily be deemed to be interrupted by the insanity of the deserting spouse.

Sir HARRY HYLTON-FOSTER, the Solicitor-General, welcomed the Bill and promised the Government's support and help to its sponsors. He admitted that a difficulty might arise when a voluntary patient released himself, perhaps unwisely, and remained at liberty for more than the permitted 28 days. But to substitute some standard other than a period of uninterrupted care and treatment as a ground of divorce would be a large change in the law and would have to await legislation arising from the Royal Commission's recommendations as a whole.

Obituary

EDWARD ROLAND THOMPSON
M.B. Edin.

Dr. E. R. Thompson, who died on Nov. 20 at the age of 75, had practised in Crewkerne, Somerset, for nearly thirty years. He was born at Amoy, China, where his parents were missionaries, but he returned to England at the age of two and he was educated at Hymers College, Hull, and at Edinburgh University, graduating M.B. in 1906. After holding house-appointments at Wolverhampton General Hospital and at Birmingham Infirmary he became an assistant in a general practice at Farnworth, Lancashire. After a trip to the Far East he returned to Farnworth as a partner in the same practice. During the 1914–18 war he served in the R.A.M.C. in Salonika and the Middle East, and after the armistice he was on the staff of General Sir George Milne and was mentioned in despatches.

In 1929 he married Mrs. H. M. Hodge, and he moved the following year to Crewkerne, where he worked in general practice in partnership with his stepsons, Dr. R. Sessions Hodge and Dr. G. S. Hodge. Dr. Thompson was M.O.H. for Crewkerne and was on the staff of Crewkerne Hospital. He was a founder member of the West Somerset Medical Club. His wife died last year.

R. S. H. writes:

Roland Thompson's salient characteristic was his matchless integrity. In his work and his play—and he had been an outstanding tennis-player before his eyesight began to fail—he gave always of his best and expected no less of his associates. He made no distinction between people—folk in need were his care: his uncompromising sense of essential values never deserted him and he had no truck with humbug. A commanding figure in any company, his reserve cloaked a human personality with wide interests. He had the gentleness, neatness, and meticulous care for small things of many big men: he was especially gentle with children and flowers, and a corm of cyclamen brought from the Struma Valley in the 1914–18 war now spreads in the wood of his garden at Crewkerne. His patients trusted him for his skill and unfailing care and loved him for his wisdom and understanding: his flowers throve—possibly for the same reasons. He leaves us with the memory of a man of principle—an upright and a fearless gentleman.

MANFRED SAKEL
M.D. Vienna

Dr. Sakel, who in 1928 at the Lichterfelde Hospital in Berlin for the first time used insulin shock therapy in schizophrenia, died in New York on Dec. 3 at the age of 57.

He was born in Nadvornaya, Austria, into a rabbinical family descended from the philosopher and physician Maimonides. He studied medicine in Brno and in Vienna, where he qualified in 1925. For the next eight years he worked in Berlin, till in 1933 he returned to Vienna as an associate in neuropsychiatry at the University Hospital. Since 1936 he had practised in the United States.

Of Sakel's original use of insulin shock therapy a colleague writes:

The type and the duration of hypoglycæmia he applied were at the time considered a dangerous complication of an overdose of insulin in diabetics. When he discovered that it had a favourable influence on the acute psychotic state, he was bold enough to repeat the treatment daily, to extend it over weeks, and finally to organise it into a well-ordered regime which is still unchanged in principle. He believed that the hypoglycæmia produced by insulin was an unsurpassed method of psychotic therapy. The procedure was entirely empirical, and his own theory of it did not stand up to scientific scrutiny. He tended to over-estimate his results and he made no effort to elaborate its theoretical foundations and the mechanism of its action. This was, however, done by others, and the work of Himwich, Gellhorn, and Hoagland in the United States, and of Georgi and Max Müller in Switzerland, was based on observations of his method. He inaugurated the period of active somatic treatment of the many psychiatric patients from whom the chronic population of our mental hospitals is recruited.

Sakel's is still the therapy of choice in early schizophrenia, shortening the acute attack and improving the quality of remissions in a good number of patients. But it does not prevent relapse and final chronicity, and it is costly and requires a great deal from the doctor and other attendants. Yet even when we have found a drug which will give as good results as hypoglycæmia, Sakel's bold use of his discovery will remain a landmark.

GEORGE CHARLES BERG
M.D. Lond., D.P.M.

Dr. Charles Berg, consulting psychiatrist to the British Hospital for Functional Nervous Disorders, died at his home in London on Dec. 5, at the age of 65.

He was born in India, at Simla Hill, and was educated at Bishop Cotton School and at Lausanne. He studied medicine at St. Thomas's Hospital and qualified in 1915. He held resident appointments there and served during the 1914–18 war as a captain in the R.A.M.C. before he graduated M.B. in 1921. He held clinical assistantships in the mental diseases department at St. Thomas's and at the Bethlem Royal Hospital before he took the M.D. and the D.P.M. in 1927. Later he joined the staffs of the Institute for the Scientific Treatment of Delinquency and the Tavistock Clinic, as well as of the British Hospital for Functional Nervous Disorders. His writings included *Clinical Psychology*, *Deep Analysis*, *War in the Mind*, *The Unconscious Significance of Hair*, and *The First Interview with a Psychiatrist*. This year he published his autobiographical *Being Lived by My Life*, and during his last illness he was completing a survey of the development of the human mind.

P.F. writes:

Charles Berg had an insatiable appetite for work. He was a man with a dynamic character who had much to give, and gave it without stint. Nervous people have gained from his books much help and insight into the cause of their suffering. His colleagues will remember him as a warm-hearted and generous man, and a skilful and much-loved physician.

Dr. Berg married twice; by his first marriage he had a son and a daughter, and by his second, in 1946 to Ruth Santo, two daughters.

Appointments

CUMMING, R. P., M.B. Aberd., F.R.C.S.E.: consultant surgeon, Shetland Islands.

FLAVELL, GEOFFREY, F.R.C.S., M.R.C.P.: consultant thoracic surgeon, Royal Masonic Hospital, London.

Notes and News

TRANSATLANTIC DISCUSSION

LONDON, Philadelphia, and Bethesda, Maryland, were linked on Dec. 4 in a three-cornered conference on the chemotherapy of cancer. The new undersea cable made possible this transatlantic exchange of views. At the Royal Society of Medicine in London the British panel included Mr. A. Dickson Wright, Prof. A. Haddow, Dr. R. Bodley Scott, Dr. J. F. Wilkinson, and Dr. Eve Wiltshaw. At the annual clinical meeting of the American Medical Association in Philadelphia the contributors were Dr. L. M. Tocantins (Jefferson Medical College), Dr. Joseph Burchenal (Cornell), Dr. R. P. Custer (Pennsylvania School of Medicine), Dr. Sidney Farber (Harvard), Dr. Emil Frei (National Cancer Institute), and Dr. Howard Skipper (Alabama Medical College). The discussion was also heard at the National Institutes of Health, Bethesda. The conference, sponsored by the A.M.A. and the R.S.M. in cooperation with Smith Kline and French Laboratories, marked the 125th anniversary of the description of lymphadenoma by Thomas Hodgkin.

MEDICAL WAR RELIEF FUND

THE committee of the Medical War Relief Fund on Oct. 10 approved a report by the distribution subcommittee on its work in the year ended Aug. 31. Seven educational grants amounting to £520 and seven maintenance grants totalling £382 had been made. The work of the Fund is decreasing; and it is expected that existing resources will enable the seven children now being helped to complete their education.

MEDICAL FILM

A NEW film, *The Reduction of Hæmorrhage During Surgery* (35 mm. and 16 mm., sound, colour, 30 min., Britain, 1957) made by the department of anæsthetics, Westminster Hospital, was shown at the annual meeting of the Association of Anæsthetists in London on Dec. 6.

The commentary states that hæmorrhage can be reduced by deep anæsthesia. Next the action of ganglion-blocking agents for controlled hypotension is shown on diagrams. The site of action of trimetaphan ("Arfonad") is proved in a cat experiment, and the clinical use of the drug both as a 0·1% infusion and by intermittent injections of a 5% solution during surgery is demonstrated. The operations shown include thyroidectomy, prostatectomy, excision of a coarctation of the aorta, lumbodorsal sympathectomy, nephrectomy, plastic surgery on the face, and a radical mastectomy; and the blood-pressure, plotted on a Nosworthy card, is shown in each case. The film ends with the warning that controlled hypotension must be employed with care, and only when there are urgent indications for it; and a list of contraindications is given.

Surgeons will approve of the operative details, but anæsthetists would like rather more precise information—for instance, the name of the drug and the dose used for the induction of the patient demonstrated. The photography is good but the colour poor; the commentary is informative, but the sound is spoilt by scraps of speech and noises from activities not included in the picture.

Copies of the film may be obtained on free loan from Roche Products Ltd., 15, Manchester Square, London, W.1.

University of Cambridge

To lighten the work of the regius professor of physic the new post of dean of the postgraduate medical school is to be created, and the general board of faculties has proposed Dr. Leslie Cole as the first holder.

National University of Ireland

On Dec. 5 the degree of M.D. was awarded to R. E. Steiner.

The following part-time lecturers have been appointed in University College, Cork:

Dr. Victor Dillon, Dr. Jeremiah Murray, Dr. Andrew Whelton (medicine); Dr. J. B. Kearney, Dr. R. C. Sutton (obstetrics and gynæcology); Mr. St. J. G. O'Connell (orthopædic surgery); Mr. John Kiely, Dr. Edmond Donovan, Mr. John Kelly (surgery).

British Association of Plastic Surgeons

The following officers have been elected: president, Mr. J. S. Tough; hon. treasurer, Mr. R. P. Osborne; new members of council, Air Commodore G. H. Morley and Mr. Mortimer Shaw.

Eugenics Society

The Galton medal has been awarded to Dr. C. P. Blacker, who was general secretary of the society from 1931 to 1952 and who is now honorary secretary. This is only the second award of the medal which the society has ever made.

Association of Anæsthetists of Great Britain and Ireland

At the 25th anniversary dinner held in London on Dec. 5, Mr. D. Walker-Smith, the Minister of Health, spoke of what the Association had done to raise the status of anæsthetics and its practitioners. In these 25 years three university chairs had been founded, and since 1949 there had been a 60% rise in the number of consultant anæsthetists, working on equal terms with other members of the medical team. Dr. T. Cecil Gray, the president, said that in 1932 Liverpool had two specialists in anæsthetics, and there were only fifty in the whole country. The responsibility for development lay on a few determined pioneers: he named Ivan Magill, H. W. Featherstone, and Ashley Daley among others. The presidency of A. D. Marston had started a new epoch with the establishment of the Faculty of Anæsthetists which gave the specialty an academic stamp and status equal to any other. With the anæsthetics section of the Royal Society of Medicine and the anæsthetics group of the British Medical Association, it formed a trinity, whose one aim was the good of the patients. For the national congress now in progress, close on 500 people had registered. Difficulties and even dangers lay ahead, and the Association must be strong and united with all in the profession who wished the National Health Service to be as good as possible—which could be achieved only by maintaining the status of every doctor, general practitioner as well as specialist. Dr. Vernon Hall, most skilfully proposing The Guests, wondered in whose style he should portray them—Hogarth's? He welcomed the Minister of Health as the seventh since the Conquest: according to precedent, when Mr. Walker-Smith had spent a short time sharpening his teeth on the doctors, it would be time for him to have a go at the T.U.C. Responding, Prof. Henry K. Beecher, of Boston, said that "the shortest way to wherever you want to go is through Great Britain," and Dr. C. R. Ritsema van Eck, vice-president of the World Federation of Anæsthetists, expressed thanks to British anæsthetists for teaching us to "use our nice new guns."

McGill University, Montreal

The faculty of medicine of this university has received a grant of $30,000 from the Markle Foundation to move the Osler library to the Medical Sciences Centre, and a grant of $22,500 for cataloguing the library and related historical material.

British Tuberculosis Association

This association offers a prize of £50 for unpublished work on tuberculosis by a member. Joint entries will be accepted. Entries must be received by Oct. 1. Further details may be had from the administrative secretary, 59, Portland Place, London, W.1.

European Organisation for Research on Fluorine and Dental Caries Prevention

This congress will take place in Brussels from May 30 to June 1, 1958. The chairman of the organising committee is Dr. M. Joachim, 67, Rue de Trèves, Brussels, Belgium.

Prof. Brian Maegraith has received the centenary award of the Bernhard Nocht medal.

Surgeon Lieut.-Commander A. P. Curtin, M.B., R.N.V.R., has been awarded the Resistance Star for Eastern Asia 1942–45 for services to Netherlands prisoners of war in Japan during the war.

Diary of the Week

DEC. 15 TO 21

Monday, 16th

HUNTERIAN SOCIETY
8.30 P.M. (Talbot Restaurant, E.C.2.) Dr. Peter Bishop, Dr. F. Dudley Hart: Use and Abuse of Cortisone.

MANCHESTER MEDICAL SOCIETY, University of Manchester
9 P.M. *General Practice.* Dr. Donald Longson: Cortico-steroids.

Wednesday, 18th

ROYAL SOCIETY OF MEDICINE, 1, Wimpole Street, W.1
5 P.M. *Comparative Medicine.* Dr. H. Smith, Mr. E. C. Hulse, Dr. Joseph Ungar: Recent Developments in Immunisation against Bacterial Disease.
8.15 P.M. *General Practice.* Dr. John Sanctuary: The Breast in Pregnancy and Lactation.

Thursday, 19th

ROYAL SOCIETY OF MEDICINE
4.45 P.M. *Dermatology.* Dr. C. Astley Clarke: Neoplasms of the Gastro-intestinal Tract associated with Inherited Abnormalities of the Skin.

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— William Withering, M.D., 1785

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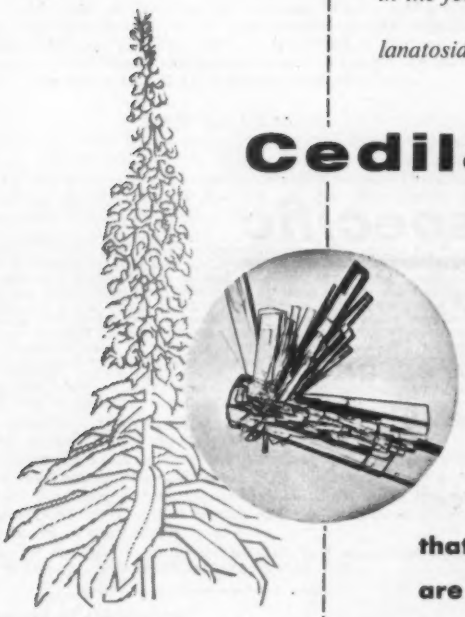

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SOLUTION	1 ml. (approx. 30 drops) contains 1 mg. lanatoside C
AMPOULES	2 ml. contain 0.4 mg. desacetyl-lanatoside C

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CALCIUM PENICILLIN-V

proved in performance the most efficient oral penicillin

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* **Ready prepared**
* **Stable**
* **Palatable**

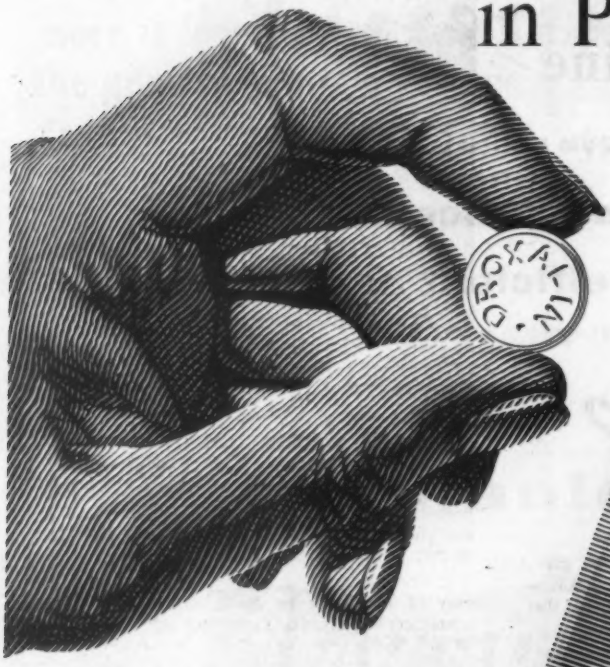
Contains 60 mg. Penicillin V
(as calcium salt) in 5cc. Bottles of 60cc. with plastic spoon.
Basic N.H.S. Price 5/6d.

Also available—
Tablets of 60 mg. and 120 mg. Penicillin V.

Detailed literature and sample gladly sent on request

BOOTS PURE DRUG COMPANY LIMITED · NOTTINGHAM · ENGLAND

DROXALIN palatability in Peptic Ulcer



IN PEPTIC ULCER, carefully regulated medication is often interrupted by the patient's distaste for an acid adsorbent. Bland and palatable, DROXALIN TABLETS overcome this difficulty and are widely prescribed in the treatment of Peptic Ulcer, Hyperacidity and Sickness of Pregnancy.

DROXALIN combines the two most preferred acid adsorbents—Aluminium Hydroxide and Magnesium Trisilicate. Pleasantly flavoured, the DROXALIN TABLET commands the patient's ready acceptance, being free from grittiness or the metallic taste usually associated with Aluminium Hydroxide therapy.

DROXALIN gives quick relief from pain by rapid acid adsorption* without danger of secondary acid rise or other harmful side effects. The special film packing enables DROXALIN to be carried hygienically in pocket or handbag.

Active ingredients per tablet:
Gelat. Alumin. Hydrox. Sicc... 2.5 grains Mag. Trisil... 2.5 grains.

**This will neutralise 50 mls. of N/10 HCl in thirty minutes.*

DROXALIN tablets are hygienically packed in film strips of 6, in cartons of 30 and dispensing packs of 504. Prescribable on E.C.10. Basic N.H.S. cost 2/2 for 50 tablets.

DROXALIN

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VITAMINS LIMITED

"British medicine is the cheapest in the world"

Vitamins Beat Inflation

The Annual General Meeting of Vitamins Ltd., was held in London in September.

The Chairman Mr. H. C. H. Graves said that net Group Trading Profit for 1956-7 after providing for taxation was £190,409 (£106,169).

The suggestion that if the National Health Service floundered on the financial rocks, it would be due to the high cost of drugs was the reverse of the truth: many standard drugs cost the Exchequer more than the corresponding proprietary. He would go farther by stating that British medicine was the cheapest in the world.

It had nothing to fear from the European Free Trade Area. He would also venture to say that the British peoples were the healthiest in the world—they were certainly never healthier. Was this realised by the man in the street? Did he realise when he paid his shilling for a prescription that he was buying the finest that medicine could provide at the cheapest cost—now and ever? He may have gazed in wonder at the name of a new drug which saved his life or the life of his nearest and dearest, but he seldom connected this with the name of the Pharmaceutical Industry of this country and the leading place its discoveries had earned it in the world of scientific research. Mr. Graves was proud of his Company's contribution to the high renown of the Pharmaceutical Industry.

SOME PRICES EVEN REDUCED

At one time we seemed to get a twist of the inflationary spiral in alternate years. It now seemed to be in alternate months. The rhythm reminded him of the well known dance band leader's—"slow, slow, quick, quick, slow." The inflationary rhythm would seem to be "coal, transport, gas, electricity, wages"—"coal, transport, gas, electricity, wages"—interrupted only by an occasional discordant bump when postal and telephone charges and such-like were added. In such an atmosphere the Company could fairly congratulate itself on not only holding its prices stable, but in many cases—materially reducing them. The main products—Vitamins, the subject of the Company's name were cheaper than ever before and it was clear, therefore, that their excellent results had certainly not been achieved by taking part in the inflationary rhythm.

The role of Bemax, as the best-known vitamin-mineral-protein food in the world, continued to be appreciated and understood by doctors and dietitians, by nurses and mothers as it had been for over a quarter of a century past.

If, like some regimes, Bemax were unpleasant and not easy of acceptance he could understand there being abstainers from its use. On the contrary, Bemax with milk or fruit juice, in soup or sprinkled on cereal foods was so delicious and added such zest to life that he really found it incredible that anyone who had the opportunity should fail to give it a trial, and still more incredible to think anyone, these days, could be found to deny their children its benefits and the protection which it afforded.

The report and accounts were adopted.

* * *

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Vitavel Syrup is a preparation containing the four principal vitamins—A, B_1, C & D—in an orange juice base with liquid glucose added. There is no smell or taste of fish oils.

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Here, in a simple preparation, are the vitamins and minerals needed in higher concentration during pregnancy—the potency of each bearing a definite relation to the daily need.

THE B-COMPLEX

Three preparations containing the most important factors of the B-complex in three levels of concentration for conditions ranging from mild debility to serious vitamin deficiency.

PARENTROVITE

An injectable preparation combining massive doses of the vitamin B-complex and vitamin C for the treatment of delirium, coma and psychosis from drugs and toxic infections.

And a complete range of single and multiple vitamin preparations.

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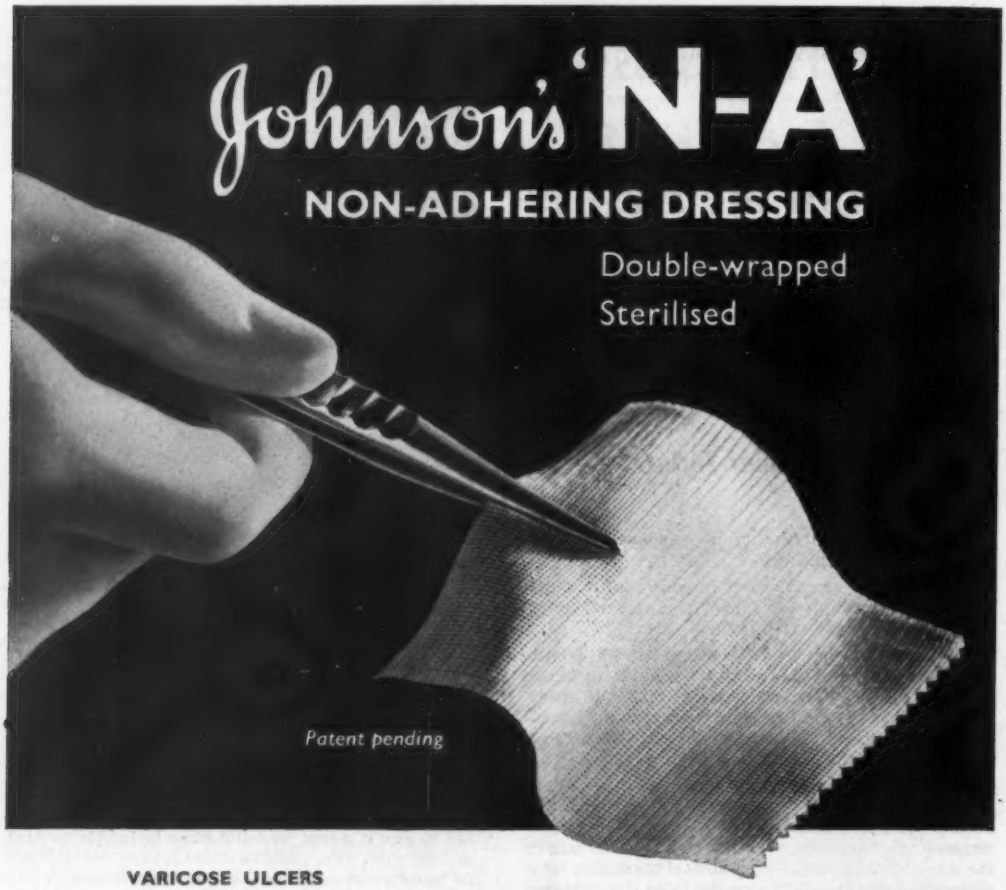
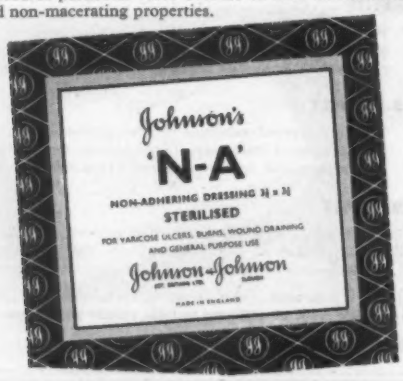


VARICOSE ULCERS

The non-adhering properties of Johnson's 'N-A' Dressings, used in conjunction with Gauze and JOHNSON'S POROUS ELASTIC ADHESIVE BANDAGES, prevent healthy granulating tissues from being disturbed when wounds are re-dressed. Dressing needs to be done less often and healing is quicker. The free passage of exudates is facilitated and there is no maceration of tissues.

BURNS AND GENERAL PURPOSES

Johnson's 'N-A' dressings have been used in burn treatment and also for cuts and abrasions for which they have proved of particular value because of their non-adhering and non-macerating properties.



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ALLOWS FREE DRAINAGE
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Johnson's 'N-A' Dressing is a pure rayon dressing which is non-adhering. This property, together with the essential requirement of allowing free drainage of exudates (resulting in freedom from maceration), makes this dressing superior to traditional materials. Johnson's 'N-A' Dressings are sterilized, unmedicated, and do not disturb healing tissues.

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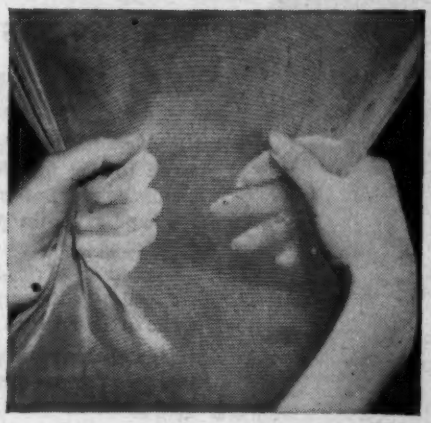

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Safe Sedation of infants

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Aneurin. Hyd. B.P. . . .	1 mg.
Potass. Bromid. B.P. . . .	60 mg.
Chloral Hydrat. B.P. . . .	60 mg.

in each fluid drachm

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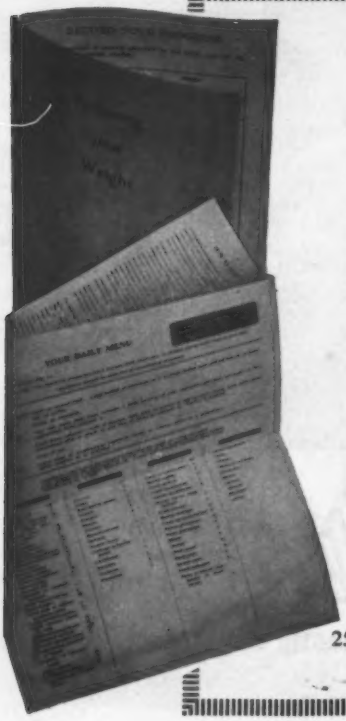

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Selective enough to avoid the side effects resulting from unwanted anticholinergic action outside the gastro-intestinal tract.
Safe enough to permit the broad range of dosage so necessary if therapy is to be truly individualized.

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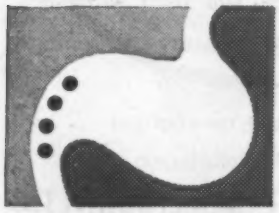

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The Terms and Conditions of Service of Hospital Medical and Dental Staff apply to all N.H.S. hospital posts we advertise, unless otherwise stated. Canvassing disqualifies, but candidates may normally visit the hospital by appointment.

Academic and Educational

ROYAL COLLEGE OF SURGEONS OF ENGLAND

COURT OF EXAMINERS

Notice is hereby given that the Council on 13th February, 1958, will elect 3 Members of the Court of Examiners, 2 to examine in General Surgery, and 1 in Otolaryngology.

The Examiner retiring in rotation in Otolaryngology (Professor V. F. Lambert) is applying for re-election.

Examiners in Surgery who have retired in rotation during the past 12 months are Mr. A. W. KENDALL, Mr. E. L. FARQUHARSON and Mr. G. QVIST.

Fellows of the College desirous of becoming candidates for the office must make application, in writing, to the Secretary on or before 1st January, 1958. KENNEDY CASSELS, Secretary.

Lincoln's Inn-fields, London, W.C.2.

GUY'S HOSPITAL MEDICAL SCHOOL, S.E.1

SIR ALFRED FRIPP MEMORIAL FELLOWSHIP

Applications are invited for the Sir Alfred Fripp Memorial Fellowship in Child Psychology tenable at Guy's Hospital. The fellowship is open to medically qualified men or women under the age of 35, preferably with experience in pædiatrics as well as in psychological medicine. Stipend £250 p.a. The appointment is for 2 years and may be held concurrently with a part-time appointment at Guy's or elsewhere.

Applications should be forwarded to the Dean (from whom copies of the regulations may be obtained), together with the names of 3 referees, not later than 31st December, 1957. Candidates should submit with their applications particulars of their previous career and a definite scheme of advanced study or research to be carried out during tenure of the Fellowship.

ROYAL FREE HOSPITAL SCHOOL OF MEDICINE

Applications are invited from graduates of the School for (*a*) the A. B. CUNNING PRIZES of the value of £30 and £20 for an essay of approximately 3000 words on the subject of "Nutrition and Pregnancy" (open only to graduates who have registered within 3 years of 1st May, 1958); (*b*) the CHARLOTTE BROWN PRIZE of £40 for an essay or published paper on a clinical research project carried out by the applicant; and (*c*) the FLORENCE STONEY PRIZE of £25 for an essay or published paper on the applicant's research work in connection with cancer.

Details should be obtained from the Secretary at the School, 8, Hunter-street, W.C.1, before entries are submitted. Closing date 1st May, 1958.

INSTITUTE OF ORTHOPÆDICS

PROVISIONAL PROGRAMME

A COURSE OF LECTURES on "Disorders of the Spine" will be given in the Lecture Room at the Institute of Orthopædics, Royal National Orthopædic Hospital, 234, Great Portland-street, London, W.1, on FRIDAYS at 6 P.M. on the following dates:—

17th Jan.	Scoliosis I	Mr. J. I. P. JAMES
31st Jan.	Scoliosis II	Mr. J. I. P. JAMES
7th Feb.	Spondylolisthesis	Mr. P. H. NEWMAN
14th Feb.	Ankylosing Spondylitis	Mr. D. TREVOR
21st Feb.	Infections of the Spine other than Tuberculosis	Mr. C. W. MANNING
28th Feb.	Disc Lesions	Mr. P. H. NEWMAN
7th March	Osteoporosis of the Spine	Dr. R. NASSIM
14th March	Tumours of the Spine	Mr. H. J. BURROWS
21st March	Pott's Disease	Mr. J. A. CHOLMELEY
28th March	Pott's Paraplegia	Mr. H. J. SEDDON

The fee for the full course will be 3 guineas, or for a single lecture 7s. 6d.

Tickets may be obtained on application to the Dean, at 234, Great Portland-street.

AMENDED DATES

L.M.S.S.A.

FINAL EXAMINATION: MEDICINE, 13th January, 10th February, 10th March, 1958. SURGERY, 13th January, 10th February, 10th March, 1958. MIDWIFERY, 14th January, 11th February, 11th March, 1958. PATHOLOGY, 14th January, 11th February, 11th March, 1958. MASTERY OF MIDWIFERY, May and November. DIPLOMA IN INDUSTRIAL HEALTH, July and December.

For regulations apply REGISTRAR, Apothecaries Hall, Black Friars-lane, London, E.C.4.

UNIVERSITY OF TORONTO

FELLOWSHIPS IN MEDICAL RESEARCH AND IN PREVENTIVE MEDICINE

The Col. Sir Albert Gooderham Memorial Fellowship in the Connaught Medical Research Laboratories, University of Toronto.

The Fitzgerald Memorial Fellowship in the School of Hygiene, University of Toronto.

Available to graduates in Medicine or Science—stipends up to $5000 p.a.

For information write to the Director, Connaught Medical Research Laboratories or the Director, School of Hygiene, University of Toronto.

UNIVERSITY OF BRISTOL. Applications are invited for an appointment as DEMONSTRATOR IN PATHOLOGY. Salary scale at present £900–£50–£1100 p.a., according to qualifications and experience. The duties include assistance with the teaching of medical and dental students and general pathology for veterinary students, and the conduct of autopsies. Facilities for research and experience of diagnostic histology are available.

Applications, giving full name, age, qualifications, details of education and experience together with the names of not more than 3 referees, should reach the undersigned, from whom further particulars may be obtained, on or before 11th January, 1958.

H. C. BUTTERFIELD, Registrar and Secretary.

GLASGOW POST-GRADUATE MEDICAL EDUCATION COMMITTEE

COURSE IN PSYCHOLOGICAL MEDICINE

A 2 term part-time Course has been organised to run during the Candlemas (6TH JANUARY–15TH MARCH) and Whitsun (15TH APRIL–21ST JUNE) terms, 1958. The Course is designed to supply formal training for graduates who intend to specialise in psychiatry, but is open to all registered medical practitioners. The instruction will amount to 10 hours per week given on MONDAY, TUESDAY and THURSDAY afternoons and SATURDAY mornings. During the Candlemas term, instruction will be provided in disciplines basic to psychiatry. During the Whitsun term, instruction will be on clinical subjects and students will attend various psychiatric hospitals. The fee for the Course is £35.

For further details, application should be made to the Director of Post-Graduate Medical Education, The University, Glasgow, W.2.

COUNCIL OF EUROPE

MEDICAL FELLOWSHIPS 1958

The Council of Europe is again offering a small number of Fellowships for the study of medical and surgical techniques in countries members of the Council. Fellowships will be available for at least 3 months and not exceeding 12 months. Travelling expenses and a monthly stipend will be paid by the Council.

Forms of application and further information may be obtained from the Ministry of Health, Division 5A, Savile-row, W.1. The closing date for return of completed forms of application is 15th January, 1958.

THE UNIVERSITY OF LIVERPOOL. Applications are invited for the post of Full-time RESEARCH ASSISTANT IN THORACIC SURGERY in connection with research work on the development of cardio-pulmonary by-passes, approved and financed by the Medical Research Council. The appointment will be from 1st January to 31st May, 1958, in the first instance, and may be renewed for a further year. The salary will be up to £1200 p.a. according to qualifications and experience.

Applications, stating age, qualifications and experience, together with the names of 2 referees, should be received by the Registrar, not later than 31st December, 1957.

THE UNIVERSITY OF LEEDS. Department of Obstetrics AND GYNÆCOLOGY. Applications are invited from registered medical practitioners for appointment as LECTURER in the Department of Obstetrics and Gynæcology at a salary on the scale £1200–£100–£1600–£100–£1900 p.a., according to age, qualifications and experience. Possession of the M.R.C.O.G. diploma is desirable, and credit will be given for a bent towards any particular line of research.

Applications (3 copies), stating date of birth, qualifications and experience, together with the names of 3 referees, should reach the Registrar, The University, Leeds, 2 (from whom further particulars may be obtained), not later than 6th January, 1958.

THE WELSH NATIONAL SCHOOL OF MEDICINE (UNIVERSITY OF WALES). Applications are invited for the appointment of ASSISTANT CLINICAL PATHOLOGIST in the Department of Pathology and Bacteriology. Previous experience in pathology is not essential. The appointment is a full-time one for a period of 2 years within the salary scale £900–£100–£1250 p.a., with participation in family allowance and superannuation schemes. The point of entry on the scale will depend on qualifications and experience.

Applications should be sent by 31st January, 1958, to the undersigned, from whom further particulars of the appointment may be obtained.

34, Newport-road, Cardiff. F. DODSWORTH, Secretary.

Hospital Services: Senior Appointments

NATIONAL HOSPITALS FOR NERVOUS DISEASES. Applications are invited for the appointment of PSYCHOLOGIST (whole-time) at The National Hospital, Queen-square, W.C.1. Experience in psychometric methods and research interests will be recommendations. The appointment will be for 1 year in the first instance. Salary in accordance with the Ministry of Health scale for Psychologists. Candidates with medical qualifications may apply.

Applications, giving the names of 2 referees, should be sent to the undersigned not later than 3rd January, 1958.

H. EWART MITCHELL, Secretary to the Board of Governors.
The National Hospitals for Nervous Diseases,
Queen-square, London, W.C.1.

NORTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited from qualified medical practitioners for the whole-time post of SENIOR ADMINISTRATIVE MEDICAL OFFICER at a salary of £2900–£140 (5)–£3600 p.a., subject to National Health Service (superannuation) regulations. Post vacant 1st August, 1958. The duties will be to act as adviser to the Board on the planning, organisation and staffing of the hospital and specialist services of the Region, and such administrative and executive functions as may be assigned to him.

Applications, together with the names of 3 referees, should be addressed to the Secretary of the Board (from whom further particulars of the post may be obtained) at 11A, Portland-place, W.1, by 31st December. Canvassing will disqualify.

CARDIFF. THE UNITED CARDIFF HOSPITALS. Applications are invited for the appointment of SENIOR CASUALTY OFFICER at the Cardiff Royal Infirmary. The successful candidate will also be attached to the Fracture Department of the Hospital. Non-resident appointment, to commence as soon as possible, for a period of up to 4 years. Salary on the scale £1653 15s.–£52 10s.–£1811 5s. in the fourth year.

Application forms are available from the Secretary to the Board at the Cardiff Royal Infirmary, Newport-road, Cardiff, and should be returned within 14 days of the appearance of this advertisement.

THE HOSPITAL FOR SICK CHILDREN, Great Ormond-street, W.C.1. Applications are invited for the vacancy of Tumour Research PATHOLOGIST for a period of 1 year in the first instance. The work involves experimental pathology. Salary in accordance with Senior Hospital Medical Officer scale.

Further particulars and forms of application, which should be returned by 6th January, 1958, may be obtained from the undersigned.

H. F. RUTHERFORD, House Governor and Secretary.

MANCHESTER REGIONAL HOSPITAL BOARD.

(*a*) Additional part-time (8 notional half-days weekly) CONSULTANT OBSTETRICIAN AND GYNÆCOLOGIST to the Bolton Hospital Centre, comprising Bolton Royal Infirmary, Bolton District General Hospital and associated maternity homes. Wide experience and higher qualifications essential; appointee to live in area. 24th December, 1957.

(*b*) Whole-time RESIDENT CONSULTANT PSYCHIATRIST to the Lancaster Moor Hospital (about 2500 Beds), near Lancaster. Appointee will be designated Deputy Medical Superintendent and will conduct outpatient clinics in the periphery. Wide experience and higher qualifications essential. 23rd December, 1957.

(*c*) Whole-time, NON-RESIDENT ASSISTANT CHEST PHYSICIAN (Senior Hospital Medical Officer) to the Wigan and Leigh Hospital Centre, including the tuberculosis unit at Wrightington Hospital. Previous experience of thoracic medicine and tuberculosis essential, higher qualification desirable. The appointment will be made in conjunction with the Local Health Authorities concerned, for whom the appointee will carry out duties in connection with prevention, care and aftercare of tuberculosis. 30th December, 1957.

Application forms from the Senior Administrative Medical Officer to the Board, Cheetwood-road, Manchester, 8, to be returned by the dates stated.

MANCHESTER, UNITED MANCHESTER HOSPITALS. MANCHESTER ROYAL EYE HOSPITAL, MANCHESTER, 13. SENIOR HOSPITAL MEDICAL OFFICER in Ophthalmology. Full-time, or maximum part-time, non-resident post. Previous experience in specialty essential.

Application form obtainable from F. J. CABLE, Secretary, United Manchester Hospitals, to be returned as soon as possible.

NORTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. ASSISTANT PHYSICIAN in Physical Medicine, West Herts Group. Whole-time or maximum sessions, Senior Hospital Medical Officer grade. Duties mainly at Watford Peace Memorial Hospital (208 Beds) and West Herts Hospital, Hemel Hempstead (120 Beds) which may be visited by direct appointment.

Application forms obtainable from and returnable to Secretary, North West Metropolitan Regional Hospital Board, 11A, Portland-place, W.1, before 13th January, 1958.

SHEFFIELD REGIONAL HOSPITAL BOARD. Maximum Part-time CONSULTANT RADIOLOGIST required for the Rotherham Group of hospitals.

Application form and further details from the Senior Administrative Medical Officer, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield. Forms to be returned by 4th January, 1958.

WELSH REGIONAL HOSPITAL BOARD. 2 Consultant RADIOLOGISTS are required in the Cardiff Hospital Management Committee Group, 1 of whom will be in administrative charge of the radiological services for the area. Duties include visits to several hospitals in Cardiff and neighbouring group areas. Optional whole-time/maximum part-time appointments.

Applications (12 copies), naming 3 referees, to Senior Administrative Medical Officer, Temple of Peace, Cathays Park, Cardiff, within 21 days.

WELSH REGIONAL HOSPITAL BOARD. Whole-time ASSISTANT RADIOLOGIST (Senior House Medical Officer) to serve the Caernarvon and Anglesey Hospital Management Committee, based at Caernarvon and Anglesey General Hospital, Bangor, with visits to other hospitals in the Group.

Applications (12 copies), naming 3 referees, to Senior Administrative Officer, Temple of Peace, Cathays Park, Cardiff, within 21 days.

Hospital Services: Junior Appointments

CENTRAL MIDDLESEX HOSPITAL, Park Royal, N.W.10. NORTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. SENIOR REGISTRAR for 3 half-days in the Dermatological Department. Previous experience in dermatology essential. Post now vacant. Hospital may be visited by direct appointment.

Application forms obtainable from and returnable to Group Secretary, Hospital Management Committee, at Central Middlesex Hospital, Park Royal, N.W.10, by 31st December, 1957.

CONNAUGHT HOSPITAL, Walthamstow, E.17. (123 Beds.) Applications are invited for the post of SECOND CASUALTY OFFICER with duties in the Department of Orthopædic and Traumatic Surgery (Senior House Officer grade). Recognised for F.R.C.S. Salary £819 10s. p.a. less £150 p.a. for board, lodging, &c.

Applications, with full details and copies of 2 recent testimonials, should be sent immediately to Secretary, Forest Group Hospital Management Committee, Langthorne-road, E.11.

GROUP LABORATORY, Mile End Hospital, Bancroft-road, London, E.1. RESIDENT ASSISTANT PATHOLOGISTS (Senior House Officer grade). Previous experience an advantage but not essential. Laboratory recognised for Diploma of Pathology and is well equipped with excellent training facilities. Posts vacant on 14th January and 18th February, 1958, respectively.

Applications, stating age, nationality, qualifications, experience and the names of 2 referees, to be sent to the Secretary, Stepney Group Hospital Management Committee, Mile End Hospital, Bancroft-road, E.1, not later than 21st December, 1958.

DULWICH HOSPITAL, East Dulwich-grove, S.E.22. Applications invited for appointments as HOUSE OFFICERS (general surgical duties). Recognised pre-registration posts vacant from 1st January.

Apply, giving age, qualifications and previous post (if any) details, with names of 2 referees or copy testimonials, to Group Secretary, Camberwell Hospital Management Committee, Dulwich Hospital.

GORDON HOSPITAL, Vauxhall Bridge-road, S.W.1. WESTMINSTER HOSPITAL TEACHING GROUP. Applications are invited for the post of RESIDENT SURGICAL OFFICER (Registrar grade) for 1 year in the first instance, starting early in January.

Applications (3 copies), with the names of 2 referees, should be sent to the Secretary, the Gordon Hospital, within 1 week of the appearance of this advertisement.

GUY'S HOSPITAL, S.E.1. Applications are invited from General Practitioners for the post of CLINICAL ASSISTANT in the Venereal Diseases Department, for attendance on 3 sessions per week, for 6 months in the first instance.

Applications should be lodged with the Superintendent, Guy's Hospital, as soon as possible.

HAMMERSMITH HOSPITAL AND POSTGRADUATE MEDICAL SCHOOL, Ducane-road, London, W.12. Joint appointment with the North West Metropolitan Regional Hospital Board. Whole-time REGISTRAR (orthopædic) required. Post vacant in January. Appointment tenable firstly at Heatherwood Hospital, Ascot (resident if required), studying long-term orthopædic surgery, transferring to Hammersmith Hospital and the Postgraduate Medical School (non-resident) on 1st August, 1958, studying orthopædic and traumatic surgery.

Applications, stating age, qualifications, experience, names of 2 referees, to Secretary, Board of Governors, The Hammersmith, West London and St. Mark's Hospitals, Ducane-road, London, W.12, by 28th December.

HIGHLANDS GENERAL HOSPITAL, Winchmore Hill, N.21. HOUSE SURGEON required 50 surgical beds, new operating theatre, Outpatient and Casualty Departments. Preference given to applicants seeking pre-registration post under Medical Act, 1950.

Applications, with copies of 3 testimonials and name and address of 1 referee, to Hospital Secretary.

HIGHLANDS GENERAL HOSPITAL, Winchmore Hill, N.21. HOUSE PHYSICIAN required. Preference given to applicants seeking pre-registration post under Medical Act, 1950.

Applications, with copies of 3 testimonials and name and address of 1 referee, to Hospital Secretary.

LAMBETH HOSPITAL, Brook-drive, S.E.11. South West METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited from registered medical practitioners for the post of SURGICAL REGISTRAR for general surgery and genito-urinary work. The appointment is normally for 2 years, but is subject to review at the end of 1 year. The post is resident or non-resident but, if the latter, the successful applicant will be required to sleep in on nights on duty.

Forms of application from the Group Secretary, Lambeth Group Hospital Management Committee, Renfrew-road, S.E.11, to be returned not later than 4th January, 1958.

LONDON CHEST HOSPITAL. Hospitals for Diseases of THE CHEST. 2 vacancies occur 1st February, 1958, for RESIDENT HOUSE PHYSICIAN. Appointment for 6 months, 4 in London, 2 at the Country Branch, near Letchworth, and post graded as House Officer. Duties include work in the Outpatient Department and special clinics, as well as in wards.

Applications, stating date of birth, qualifications with dates, and previous appointments held, with copies of 3 testimonials, should reach the undersigned not later than 20th December.

THOMAS BROWN, House Governor.

London Chest Hospital, E.2.

MARIE CURIE HOSPITAL, 66, Fitzjohn's-avenue, Hampstead, N.W.3. HAREFIELD AND NORTHWOOD GROUP HOSPITAL MANAGEMENT COMMITTEE. RESIDENT MEDICAL OFFICER (House Officer grade) required immediately.

Applications, with copies of testimonials, to the Administrative Officer by 24th December, 1957.

MIDDLESEX HOSPITAL and at THE NATIONAL HOSPITALS FOR NERVOUS DISEASES (MAIDA VALE HOSPITAL). Applications are invited for the appointment of NEURO-SURGICAL REGISTRAR to work at the above Hospitals (half-time at each hospital) for a period of 1 year in the first instance.

Written applications, with names of 2 referees, to the Secretary to the Board of Governors, Maida Vale Hospital, London, W.9, not later than 4th January, 1958.

MILDMAY MISSION HOSPITAL, Austin-street, London, E.2. Applications are invited for the pre-registration post of RESIDENT HOUSE PHYSICIAN/CASUALTY OFFICER, vacant on 13th January, 1958. Candidates should be in sympathy with the evangelical Christian aims of the Hospital.

Applications and references to be addressed to the Medical Superintendent as soon as possible.

SOUTH EAST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited for 2 appointments as Whole-time REGISTRAR in Orthopædic Surgery to fill vacancies in the approved trainee establishment in the following groups of hospitals:—

(1) Brighton and Lewes.

(2) Lewisham.

The appointments will be in accordance with the terms and conditions of service of hospital medical and dental staff (England and Wales), and will be for 1 year in the first instance.

Applications, giving particulars of age, qualifications and experience with relevant dates, together with the names and addresses of 2 referees, to be sent to the Secretary, Registrars Committee, South East Metropolitan Regional Hospital Board, 11, Portland-place, W.1, not later than 28th December, 1957.

SOUTH EAST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited for an appointment as whole-time SENIOR REGISTRAR in Pathology to fill a vacancy in the approved trainee establishment at the Lewisham Group of hospitals as from 17th March, 1958. The Lewisham Group laboratory is linked with other laboratories in south east London, and duties will include work for other groups. Candidates should have had general experience in pathology and possession of a higher qualification would be an advantage. The appointment will be in accordance with the terms and conditions of service of hospital medical and dental staff (England and Wales), and will be for 1 year in the first instance.

Applications, giving particulars of age, qualifications and experience with relevant dates, together with the names and addresses of 3 referees, to be sent to the Secretary, Registrars Committee, South East Metropolitan Regional Hospital Board, 11, Portland-place, London, W.1, not later than 28th December, 1957.

POPLAR HOSPITAL, East India Dock-road, E.14. Senior HOUSE OFFICER required at above Hospital. Duties are mainly in connection with the Receiving Room and Casualty Departments. Post vacant now.

Applications, giving full details, to Group Secretary, Bow Group Hospital Management Committee, 2A, Bow-road, E.3.

ROYAL LONDON HOMŒOPATHIC HOSPITAL, Great Ormond-street and Queen-square, W.C.1. Applications are invited from registered medical practitioners for the appointment of RESIDENT HOUSE SURGEON, vacant 1st January, 1958. Post recognised for F.R.C.S. examinations, and is tenable for 6 months. Candidates will be required to attend for interview.

Applications, stating age and full particulars, to Secretary.

ST. ALFEGE'S HOSPITAL, Greenwich, S.E.10. (367 Beds.) CLINICAL ASSISTANT required for 1 notional half-day session weekly, on Thursday morning, in Ophthalmic Department at above Hospital, for 1 year in first instance. Salary £183 15s. p.a.

Applications and testimonials to Secretary, Greenwich and Deptford Hospital Management Committee, at above Hospital by 23rd December.

ST. GILES' HOSPITAL, Camberwell, S.E.5. House OFFICER (orthopædic duties) required. Recognised pre-registration post vacant 1st January.

Applications, with names of 2 referees or copy testimonials, to Group Secretary, Camberwell Hospital Management Committee, Dulwich Hospital, East Dulwich-grove, S.E.22.

ST. MARY ABBOTS HOSPITAL, Marloes-road, Kensington, W.8.

HOUSE PHYSICIAN. 2 vacancies. Provisionally registered candidates eligible.

HOUSE SURGEON. 2 vacancies. Provisionally registered candidates eligible. Appointments recognised for F.R.C.S.

HOUSE SURGEON. Obstetrics and gynæcology. Post recognised for D.Obst.R.C.O.G. in obstetrics.

Appointments commence on 1st February, 1958. Are resident and limited to 6 months.

Applications by 27th December, 1957, on forms obtainable from Hospital Secretary. (L.114.)

ST. MARY'S HOSPITAL, Paddington, W.2. House Officer to the Almroth Wright Wards required for a period of 8 months with effect from 1st February, 1958 (first 2 months non-resident remaining 6 months resident). Remuneration at Senior House Officer rates.

Applications, stating nationality, date of birth, permanent address, qualifications with dates, details and National Health Service gradings of previous and present appointments, together with the names and addresses of 3 referees, should reach ALAN POWDITCH, House Governor, not later than 28th December, 1957.

ST. STEPHEN'S HOSPITAL, Fulham-road, Chelsea, S.W.10. HOUSE PHYSICIAN (general medicine). Resident. Post-/pre-registration. Vacancy 15th January, 1958.

Applications, naming 2 referees, to Medical Superintendent within 14 days.

THE HOSPITAL FOR SICK CHILDREN, Great Ormond-street, W.C.1. There will be a vacancy on 8th March, 1958, for an ASSISTANT MEDICAL REGISTRAR (Registrar grade).

Further particulars and forms of application, which must be returned not later than 6th January, 1958, are obtainable from the undersigned.

H. F. RUTHERFORD, House Governor and Secretary.

THE HOSPITAL FOR SICK CHILDREN, Great Ormond-street, W.C.1. There will be a vacancy on 13th March, 1958, for an ASSISTANT RESIDENT MEDICAL OFFICER (grade Senior House Officer) at the Country Branch Hospital, Tadworth, Surrey (101 Beds).

Further particulars and forms of application, which must be returned not later than 6th January, 1958, are obtainable from the undersigned.

H. F. RUTHERFORD, House Governor and Secretary.

WEST LONDON HOSPITAL, Hammersmith-road, W.6. RESIDENT CASUALTY OFFICER (Senior House Officer grading) required for 6 months from mid-January.

Applications, stating age, qualifications, experience, copies 2 recent testimonials, to Secretary, by 21st December.

WHIPPS CROSS HOSPITAL, London, E.11. Applica-tions are invited from fully registered medical practitioners for the post of HOUSE SURGEON in the Orthopædic Department. This post, recognised for the F.R.C.S., is vacant now.

Application forms from the Hospital Secretary, to be returned by 23rd December, 1957.

WOOLWICH GROUP HOSPITAL MANAGEMENT COM-MITTEE. HOUSE SURGEONS. 5 posts vacant 1st January, 3 at Memorial Hospital, Woolwich, 2 at St. Nicholas Hospital, Plumstead. All recognised for F.R.C.S., and approved for pre-registration service.

Apply to Group Secretary, Memorial Hospital, Woolwich, S.E.18.

WILLESDEN CHEST CLINIC, Pound-lane, N.W.10. NORTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. SENIOR REGISTRAR in Chest Diseases at above Clinic. Duties comprise work in Clinic, on the district, and supervision of beds in Central Middlesex Hospital, and will include teaching. Essential requirements: Higher medical qualifications and good training in general medicine. Applications from Senior Registrars in general medicine would be welcome. Appointment subject to annual review. Clinic may be visited by direct appointment.

Application forms obtainable from and returnable to Group Secretary, Central Middlesex Group Hospital Management Committee, Acton-lane, N.W.10, by 30th December, 1957.

ALTRINCHAM GENERAL HOSPITAL, Annexe and E.N.T. DEPARTMENT. (183 Beds.) SENIOR HOUSE OFFICER (surgical). This appointment affords excellent experience to suitably qualified candidates. Post recognised under F.R.C.S. regulations.

Applications, with names of 2 referees, to Group Secretary, North and Mid-Cheshire Hospital Management Committee, Sinderland-road, Altrincham.

ASHINGTON HOSPITAL. (52 Beds.) Wansbeck Hospital MANAGEMENT COMMITTEE. Applications are invited for the post of HOUSE OFFICER, becoming vacant 7th January, 1958, or possibly earlier. This is a pre-registration post and the work is predominantly surgical but some medical duties will need to be undertaken. House available for married man.

Applications, with full particulars and names of referees, to be sent as early as possible to the Group Secretary, Wansbeck Hospital Management Committee, 12, Stanley-street, Blyth, Northumberland.

ASHTON, HYDE AND GLOSSOP HOSPITAL MANAGE-MENT COMMITTEE.

SENIOR HOUSE OFFICER (obstetrics/gynæcology) required at Ashton-under-Lyne General Hospital. Bed complement 75 obstetric and 26 gynæcology. Recognised for M.R.C.O.G. Vacant February, 1958.

HOUSE OFFICER (midwifery) required. Post recognised for D.Obst.R.C.O.G., vacant February, 1958 Preference given to pre-registration candidates.

Applications, with copies of 2 testimonials, to Group Secretary, General Hospital, Ashton-under-Lyne, Lancs.

ASHTON, HYDE AND GLOSSOP HOSPITAL MANAGE-MENT COMMITTEE. 2 HOUSE PHYSICIANS required at Ashton-under-Lyne General Hospital. Vacant February, 1958. Preference given to pre-registration candidates.

Applications, with copies of 2 testimonials, to Group Secretary, General Hospital, Ashton-under-Lyne, Lancs.

BARNSTAPLE. NORTH DEVON INFIRMARY. (105 Beds.) HOUSE SURGEON (pre-registration); vacant now. The Hospital serves a wide area of pleasant countryside and the post affords good opportunity to study excellent clinical material.

Apply to Group Secretary, 19, Alexandra-road, Barnstaple.

BEBINGTON, CHESHIRE. CLATTERBRIDGE HOS-PITAL. CENTRAL WIRRAL GROUP. HOUSE OFFICER (pædiatrics), for unit of 82 Beds. Recognised pre-registration and D.C.H. 6 months commencing 1st March, 1958. Salary according to previous posts held.

Application forms obtainable from Hospital Secretary, to be returned by 18th December, 1957.

BECKENHAM HOSPITAL, Kent. Casualty Officer (Senior House Officer) required 1st January for 1 year in first instance, with duties in Orthopædic and Fracture Departments. Recognised for F.R.C.S.

Apply, stating age, nationality, qualifications, and experience, and naming 3 referees, to Administrative Officer.

BECKENHAM HOSPITAL, Kent. (100 Beds.) House SURGEON required immediately. Recognised for F.R.C.S. Pre-registration post.

Apply, stating age, nationality, qualifications, and experience, and naming 3 referees, to Administrative Officer.

BEDFORD GENERAL HOSPITAL. (436 Beds.) Applica-tions are invited for the following posts :—

RESIDENT SENIOR HOUSE OFFICER (obstetrics and gynæcology) required early February. Hospital may be visited by direct appointment.

RESIDENT HOUSE SURGEON (obstetrics and gynæcology) required mid January. Post recognised for D.Obst.R.C.O.G.

The Maternity Unit comprises 75 obstetric and 26 gynæcological beds and the Hospital has a busy outpatient department.

Detailed applications, with copies of 2 recent testimonials, to Group Secretary, Bedford Group Hospital Management Committee, 3, Kimbolton-road, Bedford, by 18th December.

BEDFORD GENERAL HOSPITAL. (436 Beds.) Applica-tions are invited for the following posts :—

HOUSE SURGEON post, vacant immediately. Pre- or post-registration ; recognised for F.R.C.S. Post offers exceptional opportunities for general experience in busy acute surgical units.

ORTHOPÆDIC HOUSE SURGEON post, vacant immediately. Pre- or post-registration ; recognised for F.R.C.S. Post offers wide experience in a busy specialist orthopædic and traumatic unit.

Applications, stating age, qualifications, experience, copies of 2 recent testimonials, to Group Secretary, Bedford Group Hospital Management Committee, 3, Kimbolton-road, Bedford.

BEVERLEY, YORKSHIRE. WESTWOOD HOSPITAL. (229 Beds.) HOUSE PHYSICIAN (House Officer or Senior House Officer grading according to experience).

Apply Group Secretary.

BIRMINGHAM ACCIDENT HOSPITAL, Bath-row, BIRMINGHAM, 15. (215 Beds and 8 House Surgeons.) HOUSE SURGEONS (resident). Vacant January/February. Hospital is largest traumatic unit in country and treats over 50,000 new patients each year. Recognised for purpose of casualty by R.C.S. (Eng.). Teaching programme by consultant staff. 6-month appointment, some of which may be spent in 42-Bedded Medical Research Council's Burns Unit.

Apply, naming 2 referees, to Administrator.

BIRMINGHAM, 18. DUDLEY ROAD HOSPITAL. (775 Beds.) 3 HOUSE PHYSICIANS (general medicine). Recognised for pre-registration. Vacant 13th January, 1st and 20th February, 1958. Each appointment is responsible for approximately 80 Male and Female adult medical beds in a unit of General Medicine under control of 2 Consultant Physicians.

Applications, marked "House Physician," enclosing copies of 3 recent testimonials, to Group Secretary.

BIRMINGHAM, 18. DUDLEY ROAD HOSPITAL. (775 Beds.) 2 HOUSE SURGEONS (general surgery). Recognised for pre-registration and F.R.C.S. Vacant 4th and 8th January, 1958. Each appointment is in a unit of approximately 85 adult and children's general surgical beds under control of 2 Consultant Surgeons.

Applications, marked "House Surgeon," to Group Secretary, enclosing copies of 2 recent testimonials.

BIRMINGHAM, 29. SELLY OAK HOSPITAL. (Equipped beds 955.) Applications are invited for the post of SENIOR HOUSE OFFICER (pædiatrics). Recognised for D.C.H.

Applications, stating qualifications, experience and age, with copies of 3 testimonials, to the Medical Superintendent.

BIRMINGHAM. THE UNITED BIRMINGHAM HOSPITALS. Applications are invited for the post of MEDICAL REGISTRAR (Registrar grade). The appointment, which is tenable for 1 year in the first instance, will be served as Resident Medical Officer at the General Hospital and, subject to satisfactory review, opportunity will be given to spend a further year in the Medical Professorial Unit at the Queen Elizabeth Hospital or elsewhere in the United Hospitals. Candidates should have the M.R.C.P. (London).

Forms of application may be obtained from, and should be returned not later than 21st December, 1957, to, the Secretary, The United Birmingham Hospitals, Queen Elizabeth Hospital, Edgbaston, Birmingham, 15.

BIRMINGHAM. THE UNITED BIRMINGHAM HOSPITALS. QUEEN ELIZABETH HOSPITAL. Applications are invited for the post of MEDICAL REGISTRAR (Registrar or Senior House Officer grade). For appointment to Registrar grade candidates should have the M.R.C.P. (London). The successful candidate may be required to be resident.

Forms of application may be obtained from, and should be returned not later than 21st December, 1957, to, the Secretary, The United Birmingham Hospitals, Queen Elizabeth Hospital, Birmingham, 15.

BIRMINGHAM. THE UNITED BIRMINGHAM HOSPITALS. Applications are invited for the appointment of RESIDENT CLINICAL PATHOLOGIST (Senior House Officer grade) at the Queen Elizabeth Hospital, Birmingham. There are 4 residents attached to the Department of Clinical Pathology. In addition to affording general experience in hæmatology, bacteriology and some biochemistry, the appointment can provide opportunities for those studying for higher qualifications in medicine. The appointment is tenable for 1 year.

Application forms should be obtained from the Secretary to the Board of Governors, United Birmingham Hospitals, Queen Elizabeth Hospital, Birmingham, 15, and should be returned to him as soon as possible.

BIRMINGHAM. THE UNITED BIRMINGHAM HOSPITALS. Applications are invited for the post of RESIDENT OBSTETRIC AND GYNÆCOLOGICAL REGISTRAR for duties at the Queen Elizabeth and The Birmingham and Midland Hospital for Woman (Professorial Unit) to commence duty at the earliest possible moment.

Forms of application with details of appointment may be obtained from, and should be returned not later than 6th January, 1958, to the House Governor, Birmingham and Midland Hospitals for Women, Showell Green-lane, Birmingham, 11.

G. A. PHALP, Secretary.

BIRMINGHAM. THE UNITED BIRMINGHAM HOSPITALS. Applications are invited for an appointment in the grade of MEDICAL REGISTRAR or SENIOR HOUSE OFFICER, according to qualifications and experience. The successful candidate will have clinical duties in the Queen Elizabeth Hospital and will also have the duties and status of a part-time member of the University staff in the University Department of Experimental Pathology. The post is preferably a resident one, but if non-resident, the appointee must be prepared to undertake resident duties as required.

Forms of application may be obtained from the Secretary, United Birmingham Hospitals, Queen Elizabeth Hospital, Birmingham, 15, and should be returned by 28th December, 1957.

BIRMINGHAM, 9. YARDLEY GREEN HOSPITAL. THORACIC SURGICAL UNIT. (66 Beds.) Vacancy for SENIOR HOUSE OFFICER. No previous experience in thoracic surgery necessary.

Applications, stating age, qualifications, training and experience, together with names of 2 referees, to be addressed to Group Secretary, Yardley Green Hospital, Birmingham, 9.

BLACKBURN AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE. SENIOR HOUSE OFFICER (pathology) required for duties at Royal Infirmary, Blackburn (Group Laboratory), but may also be required for duties at Queen's Park Hospital, Blackburn, and Victoria Hospital, Accrington, at Consultant's discretion. Recognised for D.Path.

Applications, with names of 2 referees, to Group Secretary, Hospital Management Committee Office, Royal Infirmary, Blackburn.

BLACKBURN AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE. JUNIOR HOSPITAL MEDICAL OFFICER required immediately for established Geriatric Department under control of Consultant Geriatrician. There are 360 geriatric beds at Queen's Park Hospital, Blackburn, Springfield Hospital, Blackburn, and Clitheroe Hospital, Clitheroe. Accommodation for married man may be available if required.

Applications, with names and addresses of 2 referees, to Group Secretary, Hospital Management Committee Office, Royal Infirmary, Blackburn.

BLACKBURN AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE.

Royal Infirmary, Blackburn

HOUSE SURGEONS (2) required for 25th January and 1st February, 1958. Posts recognised for F.R.C.S. and approved for pre-registration purposes.

Queen's Park Hospital, Blackburn

HOUSE SURGEON required for 1st February, 1958. Post recognised for F.R.C.S. and approved for pre-registration purposes.

Apply to Group Secretary, Hospital Management Committee Office, Royal Infirmary, Blackburn.

BISHOP AUCKLAND, Co. DURHAM. The General HOSPITAL. (350 Beds.) SOUTH WEST DURHAM HOSPITAL MANAGEMENT COMMITTEE. HOUSE PHYSICIAN required. Fully registered practitioner or pre-registration candidate.

Apply, naming 2 referees, to K. G. T. LUXFORD, Group Secretary, at the above address.

BLACKPOOL. VICTORIA HOSPITAL. (354 Beds.) HOUSE OFFICER (orthopædic and traumatic surgery) required in the main acute general hospital serving the Blackpool and Fylde area. Resident pre-registration post recognised for F.R.C.S.

Applications, stating age, experience (if any) and giving the names and addresses of 2 referees, should be sent to the Hospital Secretary.

BLACKPOOL. VICTORIA HOSPITAL. (354 Beds.) HOUSE SURGEON. Resident pre-registration post available in January, in the Department of Surgery, at this modern well-equipped Hospital with excellent facilities for gaining experience. Recognised for F.R.C.S.

Applications, stating age, experience, and the names and addresses of 2 referees, should be sent to the Hospital Secretary.

BOLTON AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE.

The Royal Infirmary, Bolton (238 Beds)

RESIDENT SENIOR HOUSE OFFICER in Orthopædic Surgery. Vacant 1st February, tenable for 12 months and recognised for F.R.C.S.

RESIDENT HOUSE SURGEONS (3). Vacant 15th January, 16th January and 1st February, tenable for 6 months and recognised under pre-registration service scheme. Also recognised for F.R.C.S.

Bolton District General Hospital (607 Beds)

RESIDENT SENIOR HOUSE OFFICERS in Medicine (2). 1 vacant immediately and 1 in New Year. Both tenable for 12 months.

RESIDENT HOUSE PHYSICIANS (3). 1 vacant immediately, 1 23rd January, and 1 14th February. Tenable for 6 months and recognised under pre-registration service scheme.

RESIDENT HOUSE SURGEONS (2). 1 vacant immediately and 1 8th February, tenable for 6 months and recognised under pre-registration service scheme. Also recognised for F.R.C.S.

Applications, stating age, nationality, qualifications, experience and the names of 2 referees, to Group Secretary, The Royal Infirmary, Bolton.

BOURNEMOUTH. ROYAL VICTORIA HOSPITAL, WESTBOURNE. BOURNEMOUTH AND EAST DORSET HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the immediate appointment of SENIOR HOUSE OFFICER (resident), for E.N.T. duties. The appointment is recognised for the D.L.O. diploma and facilities are provided for studying.

Applications to the Hospital Secretary, Royal Victoria Hospital, Shelley-road, Bournemouth.

BOURNEMOUTH. ROYAL VICTORIA HOSPITAL, Shelley-road, BOSCOMBE. (494 Beds.) BOURNEMOUTH AND EAST DORSET HOSPITAL MANAGEMENT COMMITTEE. SENIOR HOUSE OFFICER (orthopædics and casualty combined), resident or non-resident, required for the end of December. The post is recognised for the F.R.C.S. examination and is normally tenable for 12 months. The Unit consists of a Registrar and 2 Senior House Officers with an additional Senior House Officer during the summer months.

Applications to the Hospital Secretary.

BRIDGEND GENERAL HOSPITAL, Quarella-road, BRIDGEND. (381 Beds.) Applications are invited for the post of SENIOR HOUSE OFFICER (anæsthetics). This hospital is recognised for the examinations of the F.A.R.C.S.

Applications, naming 2 referees, to be addressed to the Group Secretary, Mid Glamorgan Hospital Management Committee, 8, Wind-street, Neath.

BRISTOL. COSSHAM AND FRENCHAY HOSPITAL MANAGEMENT COMMITTEE. Applications invited for post of SENIOR HOUSE OFFICER in the Regional Department of Thoracic Surgery (100 Beds) at Frenchay Hospital, Bristol. The work provides experience in all branches of cardiac, œsophageal and pulmonary surgery and the appointment is recognised for the Fellowship examinations of the Royal College of Surgeons.

Applications, stating age, and experience, and naming 2 referees to be submitted to the Group Secretary.

BRIGHTON. ROYAL SUSSEX COUNTY HOSPITAL. (314 Beds.) RESIDENT ANÆSTHETIST (Senior House Officer grade) required for 1 year with interchange of duties, by agreement, at the Brighton General Hospital and other specialised units within the Brighton and Lewes Group. Vacant 21st December. Post recognised for F.F.A.R.C.S., and D.A.

Applications, stating age, nationality and experience, and naming 2 referees, to the Administrative Officer, Royal Sussex County Hospital, Brighton, 7.

BRIGHTON. ROYAL SUSSEX COUNTY HOSPITAL. SENIOR CASUALTY OFFICER (Junior Hospital Medical Officer), non-resident, required mid-December, at the above Hospital. Recognised for F.R.C.S.

Applications as locum or for permanent post, stating usual particulars and the names of 2 referees, to the Administrative Officer.

BRIGHTON. ROYAL SUSSEX COUNTY HOSPITAL. (314 Beds.) 2 CASUALTY HOUSE SURGEONS required 28th December and 22nd January. Duties include work in orthopædic and traumatic unit. Recognised for pre-registration and F.R.C.S.

Applications, stating usual particulars, and naming 2 referees, to the Administrative Officer, Royal Sussex County Hospital, Brighton.

BROMSGROVE GENERAL HOSPITAL, Worcestershire. (423 Beds.) Applications are invited for the pre-registration post of HOUSE PHYSICIAN at the above Hospital.

Applications, with the names of 3 referees, to the Hospital Secretary.

BROMSGROVE GENERAL HOSPITAL, Worcestershire. (423 Beds.) Applications are invited for the pre-registration post of HOUSE SURGEON at the above Hospital. Post vacant January, 1958.

Applications, with the names of 3 referees, to the Hospital Secretary.

BROMSGROVE GENERAL HOSPITAL, Worcestershire. (423 Beds.) HOUSE OFFICER in Obstetrics and Gynæcology required. 38 maternity, 18 gynæcological beds. Post vacant January, 1958. Recognised for D.Obst.R.C.O.G. and M.R.C.O.G.

Applications, with the names of 3 referees, to the Hospital Secretary.

BURY AND ROSSENDALE HOSPITAL MANAGEMENT COMMITTEE. HOUSE SURGEONS (3). Applications are invited for 3 pre-registration posts in general surgery which will be falling vacant during January and February, 1958. 2 of the posts are at Bury General Hospital and the third at Rossendale General Hospital.

Apply, stating age, qualifications and other details, to the Group Secretary at Bury General Hospital, Bury, Lancs.

BURY AND ROSSENDALE HOSPITAL MANAGEMENT COMMITTEE. ROSSENDALE GENERAL HOSPITAL. Applications are invited for the post of SENIOR HOUSE OFFICER (medical).

Apply, stating full details including age, experience, nationality, and names of 2 referees, to the Group Secretary at Bury General Hospital, Bury, Lancs.

CARDIFF. ROOKWOOD HOSPITAL, Llandaff, Cardiff. JUNIOR HOSPITAL MEDICAL OFFICER required. National Health Service terms and conditions.

Apply Medical Superintendent.

CARDIFF. ST. DAVID'S HOSPITAL. Senior House OFFICER required in Geriatric Unit (200 Beds) commencing 1st February, 1958.

Form of application from Group Secretary, Cardiff Hospital Management Committee, 44, Cathedral-road, Cardiff.

CARLISLE. CUMBERLAND INFIRMARY, CITY GENERAL HOSPITAL AND CITY MATERNITY HOSPITAL. Applications are invited for the following appointments which are vacant as from 1st February, 1958 :—

HOUSE OFFICERS, recognised for pre-registration purposes. Period 6 months.

3 general surgery (recognised for F.R.C.S. examination).
1 general medicine.
2 obstetrics and gynæcology (1 recognised for D.Obst.R.C.O.G. examination).

SENIOR HOUSE OFFICERS. Period 12 months.

1 general surgery (recognised for F.R.C.S. examination).
1 general medicine.
1 orthopædics.
1 E.N.T.

Apply to the Group Secretary, Cumberland Infirmary, Carlisle.

CARSHALTON. QUEEN MARY'S HOSPITAL FOR CHILDREN. (550 Beds.) SURGICAL AND ORTHOPÆDIC REGISTRAR required for duties which include shared Registrar responsibility for 120 orthopædic beds and 60 acute and general beds. Applicants are invited to visit the Hospital by appointment with the Physician-Superintendent.

Applications, which should be made on forms obtainable from the Group Secretary, should be returned by 28th December, 1957.

CARSHALTON, SURREY. QUEEN MARY'S HOSPITAL FOR CHILDREN. (A general children's hospital of 550 Beds.) HOUSE SURGEON (House Officer), resident, required for 6 months (3 months general surgery and 3 months E.N.T. and orthopædics). Recognised for D.C.H. Applicants must have completed 12 months' pre-registration service.

Applications, stating age and qualifications, together with 1 recent testimonial and the names of 2 referees, should be submitted to the Group Secretary immediately.

CHESTERFIELD. SCARSDALE HOSPITAL. Applications are invited for the post of JUNIOR HOSPITAL MEDICAL OFFICER for Geriatric Unit and for duties at Penmore Hospital. Full Consultant services. Excellent scope for doctor interested in this specialty. House available on service tenancy.

Applications, giving full particulars, with names of 3 referees, to Group Secretary, Chesterfield Hospital Management Committee, at Chesterfield Royal Hospital.

CHESTER-LE-STREET, Co. DURHAM. GENERAL HOSPITAL. (204 Beds.) HOUSE SURGEON (general surgery). Approved pre-registration appointment, and recognised under the F.R.C.S. regulations. Post vacant 1st February, 1958.

Apply, with names and addresses of 2 referees, to Group Secretary, Dryburn Hospital, Durham.

CHELMSFORD. ST. JOHN'S HOSPITAL. Resident SURGICAL OFFICER (Senior House Officer grade). Duties commence 1st January, 1958. The appointment is recognised for training for the Fellowship of the Royal College of Surgeons, and the successful candidate will gain excellent experience in General Surgery, with good opportunity for preparation for higher qualifications. A House Surgeon is in residence.

Applications, stating age, nationality, qualifications and experience, together with recent testimonials, to be sent to the Secretary, Chelmsford Group Hospital Management Committee, Chelmsford and Essex Hospital, London-road, Chelmsford.

CHELMSFORD AND ESSEX HOSPITAL. (161 Beds.) Applications are invited for the post of RESIDENT HOUSE SURGEON. Pre-registration post. The post offers good surgical experience. Recognised for the F.R.C.S.

Applications, together with 2 recent testimonials, to the Secretary, Chelmsford Hospital Management Committee, London-road, Chelmsford.

CHICHESTER. ROYAL WEST SUSSEX HOSPITAL. (202 acute beds.) SENIOR HOUSE SURGEON (Deputy Resident Surgical Officer) required at above Hospital. Post recognised for F.R.C.S. Resident staff of 6—Resident Surgical Officer, 3 House Surgeons, Resident Medical Officer, and House Physician. Salary £819 10s. p.a., less residential charge. Vacant 28th December, 1957.

Applications, stating age, experience, qualifications, with references or names of referees, to Senior Administrative Officer.

COLCHESTER GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for :—

Essex County Hospital, Colchester (185 Beds)

Post of HOUSE PHYSICIAN. First, second, third or pre-registration post, tenable for 6 months.

Essex County Hospital, Colchester (19 gynæcological beds), **Colchester Maternity Hospital** (22 obstetric beds)

Post of HOUSE OFFICER (Male or Female) (obstetric and gynæcological). First, second, third or pre-registration post, tenable for 6 months.

Black Notley Hospital, Braintree, Essex (516 Beds)

Post of HOUSE SURGEON. First, second, third or pre-registration post. Includes duties in general surgical and gynæcological wards. Recognised for F.R.C.S. Tenable for 6 months.

Applications, with copies of 3 testimonials, to Group Secretary, Colchester Group Hospital Management Committee, 14, Pope's-lane, Colchester, Essex.

COULSDON, SURREY. NETHERNE HOSPITAL. South WEST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited for the appointment of REGISTRAR (whole-time) at the above Hospital, which is recognised for the D.P.M. The Hospital has an admission-rate of 1600 a year and all modern forms of treatment are carried out. There are 4 active Outpatient Departments in general hospitals and Departments of Clinical Research, Neurosurgery, Psychology and Social Service and a modern electro-encephalographic unit. Successful candidate will be required to take up appointment on 1st April, 1958.

Application forms may be obtained from the Secretary.

COVENTRY AND WARWICKSHIRE HOSPITAL, COVENTRY. ASSISTANT PATHOLOGIST (Junior Hospital Medical Officer status) required for duties mainly at Group Laboratory. Recognised D.Path. Good opportunity for experience in all branches of specialty.

Applications, with full details and names of 2 referees, to Group Secretary, Coventry and Warwickshire Hospital, Coventry.

DERBY. DERBYSHIRE CHILDREN'S HOSPITAL. HOUSE SURGEON (pre-registration) or SENIOR HOUSE OFFICER required to commence 8th January, 1958. Post recognised for D.C.H.

Applications, stating full particulars, with names of 2 referees, to be sent as soon as possible to Secretary.

DERBY. DERBYSHIRE ROYAL INFIRMARY. (416 Beds.) SENIOR HOUSE OFFICER (orthopædic). Vacant 1st January. Recognised for 6 months' "unspecified" training for F.R.C.S.

Apply, giving full details and 2 names for reference, to Secretary.

DERBY. THE PASTURES HOSPITAL, Mickleover, DERBY (Hospital for mental and nervous disorders.) **DERBY NO. 3 HOSPITAL MANAGEMENT COMMITTEE.** JUNIOR HOSPITAL MEDICAL OFFICER required. Salary, £852 10s., rising by £55 p.a. to £1182 10s. The Hospital is near to general hospitals and facilities for obtaining D.P.M. and Membership training are available. Large outpatient system. Postgraduate training in psychiatry available at Sheffield University. House available to married person at a reasonable rent. The Hospital is pleasantly situated about 4 miles from the centre of Derby.

Applications, stating qualifications and experience and giving the names of 2 referees, to be sent immediately to the Group Secretary.

DONCASTER. WESTERN HOSPITAL. (Recognised under the Regulations for the D.Obst.R.C.O.G. and M.R.C.O.G. (obstetrical experience) and approved for pre-registration service under the Medical Act, 1950.) Applications are invited for the post of OBSTETRICAL HOUSE OFFICER (Senior House Officer or pre-registration post). Vacant late January.

Applications should be forwarded to the Group Secretary, Doncaster Hospital Management Committee, at Doncaster Royal Infirmary by 24th December.

DURHAM. COUNTY HOSPITAL. (116 Beds.) Resident HOUSE SURGEON required in Orthopædics and Casualty. Post recognised for pre-registration purposes. This post offers facilities for good and varied experience in a busy orthopædic and accident hospital which serves a wide mining and industrial area.

Apply, giving age, experience and names of 2 referees, to the Group Secretary, Dryburn Hospital, Durham.

DURHAM. DRYBURN HOSPITAL. (303 Beds.) HOUSE PHYSICIAN for Pædiatric Unit of 42 Beds. Approved pre-registration appointment and recognised for the D.C.H. Post vacant 1st February, 1958.

HOUSE OFFICER (gynæcology). Post vacant 1st February, 1958. The person appointed may be considered for a further appointment of 6 months' duration in midwifery at the end of the first appointment.

Apply, with names and addresses of 2 referees, to Group Secretary, Dryburn Hospital, Durham.

EDGWARE GENERAL HOSPITAL, Edgware, Middlesex. Locum SENIOR HOUSE OFFICER required in the Casualty Department for the period 16th–30th January, 1958.

Apply immediately to Medical Director.

EAST ANGLIAN REGIONAL HOSPITAL BOARD. MEDICAL OFFICER at Regional Blood Transfusion Centre, Brooklands-avenue, Cambridge. Duties include work in the laboratories, attendance at blood collection sessions and deputising for Medical Director. Salary on scale £935–£1061 10s. p.a.

Applications, stating age, experience and the names of 3 referees, to the Board's Senior Administrative Medical Officer, 117, Chesterton-road, Cambridge, by 28th December, 1957.

EAST ANGLIAN REGIONAL HOSPITAL BOARD. SURGICAL REGISTRARS (2) Ipswich and East Suffolk Hospital. Posts recognised for F.R.C.S. Appointments for 1 year, renewable for second year.

Applications, stating age, experience and the names of 3 referees, to the Board's Senior Administrative Medical Officer, 117, Chesterton-road, Cambridge, by 28th December, 1957. Candidates invited to visit hospital by direct arrangement with Hospital Management Committee Secretary, Ipswich and East Suffolk Hospital (Anglesea-road Wing), Ipswich.

EDINBURGH. PRINCESS MARGARET ROSE ORTHOPÆDIC HOSPITAL. Applications are invited from registered medical practitioners for an appointment as SENIOR HOUSE OFFICER (resident) in the adult wards of the above Hospital. National Health Service scale.

Applications, stating age, qualifications and experience, and names of 2 referees, to be sent immediately to the Secretary, Edinburgh Central Hospitals, 1, Rillbank-terrace, Edinburgh, 9.

EDINBURGH CENTRAL HOSPITALS. Applications are invited from registered medical practitioners and pre-registration graduates for resident appointments for 6 months commencing 1st April, 1958. National Health Service scale.

Royal Hospital for Sick Children, Edinburgh

3 HOUSE PHYSICIANS.
1 HOUSE SURGEON (E.N.T.).

Chalmers Hospital, Edinburgh

1 HOUSE SURGEON (gynæcological and children's surgical annexe).

Applications stating age, qualifications and experience, and names of 2 referees, to be sent by 21st December to Secretary, Edinburgh Central Hospitals, 1, Rillbank-terrace, Edinburgh, 9.

EDINBURGH. THE ROYAL EDINBURGH HOSPITAL FOR MENTAL AND NERVOUS DISORDERS. Applications are invited for the appointment of SENIOR HOUSE OFFICER, resident or non-resident, in this Teaching Hospital with good opportunities of training in psychiatry. Appointment for 1 year.

Applications, stating qualifications, experience and names of 2 referees, to Physician-Superintendent, Royal Edinburgh Hospital, Morningside Place, Edinburgh, 10, as soon as possible.

EPPING. ST. MARGARET'S HOSPITAL. (424 Beds.) SENIOR HOUSE OFFICER (chest diseases and casualty) required for Tuberculosis Wards in busy general hospital. 40 chest diseases beds run in conjunction with clinic within the grounds. Good experience. Modern methods of treatment. Candidate required to devote one-third of time to casualty duties. Appointment vacant 2nd February, 1958—locum appointment available for preceding fortnight.

Applications, with copies of 2 recent testimonials, to be sent to the Group Secretary, Epping Group Hospital Management Committee, "Oak Cottage," The Plain, Epping, Essex, by 18th December, 1957.

EPSOM DISTRICT HOSPITAL, Dorking-road, Epsom, SURREY. RESIDENT HOUSE PHYSICIAN required 1st February. Pre-registration post.

Applications, stating age, qualifications and experience with copies of 2 recent testimonials, should be sent as soon as possible to Group Secretary at above address.

GLASGOW NORTHERN HOSPITALS. Board of Manage-MENT. Applications are invited for a post of SENIOR HOUSE OFFICER in Obstetrics and Gynæcology at Stobhill General Hospital, Glasgow, which becomes vacant as from 1st February, 1958. The appointment will be for 1 year in the first instance.

Applications, stating age, qualifications, experience and present appointment, and naming 2 referees, to be lodged with the Secretary, 13, Woodside-place, Glasgow, C.3, by 26th December, 1957.

GLASGOW, E.3. ROBROYSTON HOSPITAL. Junior HOSPITAL MEDICAL OFFICER required. Resident or non-resident. The work carried out consists mainly of tuberculous pulmonary disease though substantial units exist for skeletal urological tuberculosis. A small unit exists for acute respiratory diseases and there are also units for non-tuberculous chest diseases and for geriatrics.

Applications should be forwarded to the Physician-Superintendent.

GREENOCK. RAVENSCRAIG HOSPITAL (Mental and General). Applications are invited for the post of RESIDENT JUNIOR HOSPITAL MEDICAL OFFICER (Male or Female). The post offers experience in all branches of psychiatry, including modern forms of treatment, and outpatient clinics. Experience is available also in the medical and geriatric wards. The hospital is recognised for the D.P.M. and facilities will be granted to attend courses in Glasgow. It is probable that married quarters will be available in the near future.

Applications, with full details, and the names of 2 referees, to be forwarded to the Physician-Superintendent.

GRANTHAM AND KESTEVEN GENERAL HOSPITAL. (118 Beds. Recognised for training for F.R.C.S.) SHEFFIELD REGIONAL HOSPITAL BOARD. SECOND RESIDENT SURGICAL OFFICER with duties in Orthopædics, Gynæcology, E.N.T. and relief duties for Resident Surgical Officer required immediately. (Registrar rate of pay.) Appointment for 1 year in first instance.

Apply to Secretary, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, by 23rd December, 1957, giving age, nationality, qualifications, present and previous appointments with dates, naming 3 referees.

GRANTHAM AND KESTEVEN GENERAL HOSPITAL. (118 Beds.) RESIDENT HOUSE PHYSICIAN (Senior House Officer or pre-registration intern). General medical and pædiatric. Post vacant 1st February, 1958.

Applications, with full details and names of 2 referees, to Secretary, 101, Manthorpe-road, Grantham.

HALIFAX. ROYAL HALIFAX INFIRMARY. House SURGEON for General Surgery required. Post vacant 10th December, 1957.

Applications to the Group Secretary, Royal Halifax Infirmary, Halifax.

HALIFAX. ROYAL HALIFAX INFIRMARY. Senior HOUSE OFFICER in Anæsthetics required. Post recognised for D.A. Salary £819 10s. p.a. less £150 p.a. for board-residence.

Applications to be forwarded to the Group Secretary, Royal Halifax Infirmary, Halifax.

HASLEMERE AND DISTRICT HOSPITAL. (82 Beds.) GUILDFORD GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from registered medical practitioners for the post of SENIOR HOUSE OFFICER (Locum considered) (surgical, with charge of 12 acute medical beds). Duties to commence 1st January, 1958. Valuable experience in general and emergency surgery, orthopædic, E.N.T., gynæcological, children and casualty work.

Applications to Hospital Secretary, Haslemere and District Hospital, Haslemere, Surrey, immediately with names of 3 referees.

HASTINGS AND ST. LEONARDS-ON-SEA. BUCH-ANAN HOSPITAL. (91 Beds.) (Obstetric, Gynæcological and Premature Baby Unit.) SENIOR HOUSE OFFICER required for Obstetric and Premature Baby Unit. Appointment, recognised for D.Obst.R.C.O.G., is vacant 17th January, 1958.

Apply, giving names and addresses of 3 referees, to Hospital Administrator.

HASTINGS. ROYAL EAST SUSSEX HOSPITAL. (150 Beds.) Applications are invited for the post of HOUSE SURGEON (pre-registration), vacant now. This Hospital is the main surgical hospital in the Hastings area and the post offers excellent experience.

Apply immediately, with 2 testimonials or names of 2 referees, to the Administrator of the Hospital.

HEMEL HEMPSTEAD, HERTFORDSHIRE. WEST HERTS HOSPITAL. HOUSE SURGEON (pre-registration) required.

Applications, giving full details and 2 names for reference, should be sent to the Hospital Secretary as soon as possible.

HEMEL HEMPSTEAD, HERTFORDSHIRE. ST. PAUL'S HOSPITAL. HOUSE PHYSICIAN (pre-registration) required, commencing date 15th January.

Applications to the Hospital Secretary, together with 2 copies of testimonials.

HENLEY-ON-THAMES, OXFORDSHIRE. PEPPARD CHEST HOSPITAL. (236 Beds.) READING AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from registered medical practitioners for the post of JUNIOR HOSPITAL MEDICAL OFFICER. The Hospital deals with all types of chest disease in medical and surgical wards. Previous experience in resident hospital appointments is desirable. Single accommodation is available.

Applications, stating age, qualifications and experience, with the names of 2 referees, should be forwarded to the Group Secretary, Reading and District Hospital Management Committee, 3, Craven-road, Reading.

HERTFORD COUNTY HOSPITAL. (171 Beds—Hospital situated 21 miles from London.) Applications are invited for the undermentioned appointments :—

HOUSE SURGEON (general), first or second post, to commence as soon as possible.

HOUSE SURGEON (general, gynæcology and obstetrics), first or second post, to commence 13th December, 1957, or as soon after that date as possible

Pre-registration posts ; recognised under F.R.C.S. regulations.

Applications to Group Secretary, Hertford Hospital Management Committee, County Hospital, Hertford, Herts.

HUDDERSFIELD ROYAL INFIRMARY. (285 Beds.) Applications are invited for the post of CASUALTY OFFICER. The post, which is resident, is recognised under the Fellowship regulations and will be graded either Junior Hospital Medical Officer or Senior House Officer according to experience. Duties terminate at 7 P.M. with 1 night weekly on call.

Applications for the appointment, which will be vacant on 23rd January, 1958, should be accompanied by copies of 3 recent testimonials and addressed to the undersigned.

H. J. JOHNSON, Group Secretary.

The Royal Infirmary, Huddersfield.

HUDDERSFIELD (near). STORTHES HALL HOSPITAL, KIRKBURTON, near HUDDERSFIELD. Applications are invited for the post of JUNIOR HOSPITAL MEDICAL OFFICER and also for a Locum Tenens JUNIOR HOSPITAL MEDICAL OFFICER for long or short period. Residential accommodation for single persons available.

Applications, giving age, experience, &c., should be sent to the Medical Superintendent immediately. E. WALSH, Secretary.

HULL. KINGSTON GENERAL HOSPITAL. (419 Beds.) HULL 'A' GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of RESIDENT JUNIOR HOUSE SURGEON (recognised for the F.R.C.S. examinations; pre- or post-registration). Busy acute general surgical unit.

Applications, with 2 recent testimonials, to the Hospital Secretary.

IPSWICH AND EAST SUFFOLK HOSPITAL (Anglesea-ROAD WING). (356 Beds.) Applications are invited for the post of HOUSE SURGEON to the Senior Consultant General Surgeon, vacant mid-January. The post is recognised for pre-registration and for the F.R.C.S. examinations.

Applications, with copies of recent testimonials, to Hospital Secretary.

IPSWICH AND EAST SUFFOLK HOSPITAL (Anglesea-ROAD WING). (356 Beds.) Applications are invited for 2 posts of HOUSE SURGEON to Consultant General Surgeons, both vacant mid-January. The posts are recognised for pre-registration and for the F.R.C.S. examinations.

Applications, with copies of recent testimonials, to Hospital Secretary.

IPSWICH. FOXHALL HOSPITAL. (102 Beds for chest diseases.) SENIOR HOUSE OFFICER. The Hospital is actively engaged in the investigation and treatment of all forms of chest disease, including major thoracic surgery and a respiratory function unit. House available.

Applications, with copies of recent testimonials, to Physician-Superintendent, from whom further details may be obtained.

KENDAL. WESTMORLAND COUNTY HOSPITAL. (82 Beds.) RESIDENT SENIOR HOUSE OFFICER (medical). Duties include the care of acute cases under the supervision of 2 Consultant Physicians, and attendance at consultative clinics. Post vacant now, and tenable for 1 year.

Applications, with full particulars and names of 2 referees, to be addressed to Group Secretary, Royal Lancaster Infirmary, Lancaster.

KIDDERMINSTER AND DISTRICT GENERAL HOSPITAL. (112 Beds.) REGISTRAR (casualty) required also to deputise for Surgical Registrar. Experience specialty essential. Higher qualification desirable. Resident or non-resident.

Application forms from Secretary, Mid-Worcestershire Hospital Management Committee, Birmingham-road, Bromsgrove, to be returned by 23rd December, 1957.

KIDDERMINSTER AND DISTRICT GENERAL HOSPITAL, WORCESTERSHIRE. (112 Beds.) Applications are invited for the pre-registration post of HOUSE SURGEON at the above Hospital.

Applications, with the names of 3 referees, to the Hospital Secretary.

KINGSTON GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from suitably qualified medical officers for the post of PÆDIATRIC REGISTRAR. The post will become vacant on 1st February, 1958. Experience in pædiatrics and D.C.H. qualification essential.

Applications, stating age, qualifications and experience, together with the names of 3 referees, should reach the Group Secretary, 35, Coombe-road, Kingston-on-Thames, within 14 days of the appearance of this advertisement.

LEEDS. THE UNITED LEEDS HOSPITALS. THE GENERAL INFIRMARY AT LEEDS. RESIDENT ORTHOPÆDIC OFFICER required of Senior House Officer status. The post will initially be for 6 months from 1st February, 1958, and will be renewable for a further period of 6 months thereafter. Terms and conditions of service for hospital medical staff apply.

Applications, stating age, qualifications, previous posts with dates, to be sent to the Secretary to the Board by not later than 20th December, 1957.

LEEDS. THE UNITED LEEDS HOSPITALS. The General INFIRMARY AT LEEDS. Vacancy exists for REGISTRAR either as Trainee Radiologist or with D.M.R. Candidates with higher qualifications in medicine or surgery preferred. Terms and conditions of service for hospital medical and dental staffs apply. The appointment will be for 1 year in the first instance and renewable thereafter.

Applications, giving details of age, qualifications, previous posts, with dates, and 3 names for reference, should be sent to the Sub-Dean, School of Medicine, Leeds, 2, by not later than 27th December, 1957.

LEEDS. THE UNITED LEEDS HOSPITALS. The General INFIRMARY AT LEEDS. REGISTRAR in Urology required for a period of 1 year in the first instance. Renewable for second year. Post offers good experience either to candidates having already embarked upon training in general surgery or to those who wish to specialise in urology. Whitley conditions of service apply.

Applications, stating age, experience, qualifications, previous posts, with dates, and 3 names for reference, should be sent to the Sub-Dean, the Medical School, Leeds, 2, as soon as possible.

LINCOLN COUNTY HOSPITAL. (200 Beds.) Applications are invited from pre-registration candidates for appointments as HOUSE SURGEONS in January and February, 1958, for 6 months, to be followed, if satisfactory, by appointment as House Physician for a further 6 months.

Full particulars should be forwarded to—

R. W. HOWICK, Group Secretary,
Lincoln No. 1 Hospital Management Committee.

LINCOLN. ST. GEORGE'S HOSPITAL. (242 Beds.) **SHEFFIELD REGIONAL HOSPITAL BOARD.** Whole-time RESIDENT REGISTRAR (pædiatrics) required. Duties include care of newborn and premature babies, exchange transfusions, neonatal surgery and duties at a maternity unit at Lincoln County Hospital. This post offers excellent opportunity for the study of metabolic diseases in childhood and infancy. A new cubicled unit is being opened. Appointment for 1 year in first instance.

Apply to Secretary, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, by 23rd December, 1957, giving age, nationality, qualifications, present and previous appointments with dates, naming 3 referees.

LEAMINGTON SPA. WARNEFORD GENERAL HOSPITAL. (197 Beds.) SENIOR HOUSE OFFICER (anæsthetics) for duties at the above Hospital. Post vacant 20th January and recognised for F.F.A. R.C.S. and D.A.

Applications to Hospital Secretary.

LEAMINGTON SPA. WARNEFORD GENERAL HOSPITAL. (197 Beds.) HOUSE SURGEON for Obstetric and Gynæcology Departments. Applications from fully registered practitioners and pre-registration applicants. Post vacant early January. Recognised for D.Obst.R.C.O.G.

Apply Hospital Secretary, together with copy testimonials.

LEAMINGTON SPA. WARNEFORD GENERAL HOSPITAL. (197 Beds.) HOUSE PHYSICIAN. Vacancy suitable for fully registered or pre-registration applicant. Post vacant.

Applications, with copies of 2 recent testimonials, to be sent to Hospital Secretary.

LANCASTER. BEAUMONT HOSPITAL, Slyne-road. PÆDIATRIC REGISTRAR (resident). Previous pædiatric experience essential. Duties include experience in children's medical ward, in neonatal unit, and pædiatric outpatient clinics. Unit recognised for D.C.H. Candidates may visit hospital by direct appointment.

Applications, together with names of 2 referees, to Group Secretary, Royal Lancaster Infirmary, Lancaster.

LANCASTER MOOR HOSPITAL, Lancaster. (Regional MENTAL HOSPITAL.) Applications are invited for the post of resident JUNIOR HOSPITAL MEDICAL OFFICER (Male or Female). Accommodation for a single medical officer but accommodation may possibly be available early in 1958 for a married applicant. Hospital recognised for D.P.M. and facilities granted for attending neighbouring universities. All modern methods of investigation and treatment carried out. Hospital serving North Lancashire and Lake District. Post for initial period of 4 years, but renewable if services satisfactory.

Apply Medical Superintendent.

LIVERPOOL AND DISTRICT EASTERN HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the following medical appointments vacant from 1st March, 1958, and tenable for 6 months :—

Broadgreen Hospital, Liverpool 14

ADMISSION ROOM AND CASUALTY OFFICER, whole-time, non-resident. Recognised for F.R.C.S. Senior House Officer status. Salary £819 10s. p.a. Hours of duty : week-days 9 a.m. to 5 p.m. and Saturdays 9 a.m. to 1 p.m.

ADMISSION ROOM AND CASUALTY OFFICER, part-time, non-resident. Senior House Officer status. Salary £372 5s. p.a. Hours of duty : mornings Monday to Friday, up to 17½ hours weekly.

2 HOUSE SURGEONS (obstetrics and gynæcology), whole-time, resident. Recognised for pre-registration but preference given to registered practitioners. Salary £467 10s.–£522 10s.–£577 10s. according to experience, less £125 p.a. for residence. Recognised by R.C.O.G.

Mill Road Maternity Hospital

3 HOUSE SURGEONS (obstetrics and gynæcology), whole-time, resident. Recognised for pre-registration but preference given to registered practitioners. Salary £467 10s.–£522 10s.–£577 10s. according to experience less £125 p.a. for residence. Recognised by R.C.O.G.

Applications, on forms obtainable from the undersigned, to be returned completed as soon as possible. H. BLYTHE,
Broadgreen Hospital, Liverpool, 14. Group Secretary.

LIVERPOOL. THE UNITED LIVERPOOL HOSPITALS. Applications are invited for temporary appointment as REGISTRAR in Radiology for the period to 30th September, 1958. The person appointed will be eligible to apply in the summer of 1958 for appointment for the year beginning 1st October, 1958.

Apply by 31st December on form obtainable from the Secretary, 80, Rodney-street, Liverpool, 1.

LOWESTOFT AND NORTH SUFFOLK HOSPITAL, LOWESTOFT. (98 Beds.) HOUSE PHYSICIAN (House Officer or Senior House Officer status). Post vacant towards end of January ; recognised for pre-registration service and the Hospital is regularly visited by Consultant Staff from the Norfolk and Norwich Hospital. The applicants should be willing to give anæsthetics of a simple nature when required. Membership of a Medical Defence Society is a condition of appointment.

Applications, giving full details with names of 2 referees, to Hospital Secretary.

LUTON AND DUNSTABLE HOSPITAL. Children's ANNEXE. REGISTRAR to the Pædiatric Department of the Luton and Dunstable Hospital, required early February. Post resident or non-resident. Children's Annexe is separate from the parent hospital, taking medical and surgical children, and recognised for D.C.H. Applicants may visit by direct appointment (Tel. Luton 978).

Application form from Secretary, Luton and Hitchin Group Hospital Management Committee, St. Mary's Hospital, Luton, Beds.

MAIDENHEAD HOSPITAL, Berkshire. Applications invited for post of HOUSE SURGEON vacant 15th December. Pre-registration post.

Applications, stating age, qualifications and nationality, with names of 3 referees, to Secretary.

MAIDENHEAD HOSPITAL, Berkshire. Applications invited for post of CASUALTY OFFICER (Senior House Officer grade), vacant 30th December. Post recognised for F.R.C.S.

Applications, stating age, qualifications, experience and nationality, with copies of testimonials or names of 3 referees, to Secretary.

MAIDSTONE. WEST KENT GENERAL HOSPITAL. (141 Beds.) **MID-KENT HOSPITAL MANAGEMENT COMMITTEE.** Applications are invited for the pre-registration post of HOUSE PHYSICIAN. 6 months' appointment. Post vacant mid-January, 1958. Salary at the rate of £467 10s.–£577 10s. A deduction at the rate of £125 a year is made for board and lodging, and other services provided.

Applications should be forwarded, as soon as possible, to the Administrative Officer at the Hospital.

MAIDSTONE. WEST KENT GENERAL HOSPITAL. (141 Beds.) **MID-KENT HOSPITAL MANAGEMENT COMMITTEE.** Applications are invited for the pre-registration post of HOUSE SURGEON. 6 months' appointment. Post vacant mid-January, 1958. Salary at the rate of £467 10s.–£577 10s. A deduction at the rate of £125 a year is made for board and lodging, and other services provided.

Applications should be forwarded, as soon as possible, to the Administrative Officer at the Hospital.

MAIDSTONE. WEST KENT GENERAL HOSPITAL. (141 Beds.) MID-KENT HOSPITAL MANAGEMENT COMMITTEE. CASUALTY OFFICER (Senior House Officer). Recognised for F.R.C.S. Salary £819 10s. p.a. less £150 p.a. for board and lodging. Post vacant February, 1958.

Applications to the Administrative Officer at the Hospital.

MANCHESTER REGIONAL HOSPITAL BOARD. Blackburn AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE. RESIDENT REGISTRAR (obstetrics/gynæcology) required 1st February, 1958. Post recognised for Membership and D.Obst.R.C.O.G. (combined obstetrics and gynæcology). Based on Queen's Park Hospital, Blackburn, a large busy hospital with 58 obstetric and 29 gynæcology beds. Duties also at Royal Infirmary, Blackburn, and Victoria Hospital, Accrington. Accommodation may be available for a married man.

Application forms available from and returnable to the Group Secretary, Hospital Management Committee Office, Royal Infirmary, Blackburn.

MANCHESTER REGIONAL HOSPITAL BOARD. South MANCHESTER HOSPITAL MANAGEMENT COMMITTEE. BAGULEY HOSPITAL (402 Beds.) The Board invite applications for the post of REGISTRAR or SENIOR HOUSE OFFICER in Chest Diseases. This Hospital is a large thoracic unit fully equipped for the medical and surgical treatment of tuberculosis and other chest diseases. Attached to the Hospital is a chest clinic. The post offers opportunities for wide experience in medical and surgical treatment of patients suffering from tuberculosis and other diseases of the chest, together with chest clinic work. Ample scope for clinical research.

Applications, stating age, qualifications, nationality, experience and the names of 2 referees, to be forwarded to the Group Secretary, Withington Hospital, Manchester, 20, within 7 days of appearance of this advertisement.

MANCHESTER REGIONAL HOSPITAL BOARD. Salford HOSPITAL MANAGEMENT COMMITTEE. HOPE HOSPITAL, SALFORD, 6. SURGICAL REGISTRAR required at the above Hospital. Post vacant 1st March, 1958. A busy general hospital offering excellent experience, recognised for F.R.C.S.

Applications, together with names and addresses of 2 referees, to be sent to Group Secretary, Salford Royal Hospital, Salford, 3, before 28th December, 1957.

MANCHESTER REGIONAL HOSPITAL BOARD. Salford HOSPITAL MANAGEMENT COMMITTEE. HOPE HOSPITAL, SALFORD, 6. ORTHOPÆDIC REGISTRAR required, 60 adult and children's beds. Duties also at Salford Royal and Royal Manchester Children's Hospitals.

Applications to Group Secretary, Salford Royal Hospital, Salford, 3, before 21st December, 1957.

MANCHESTER, 20. WITHINGTON HOSPITAL. South MANCHESTER HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the pre-registration appointments of 5 HOUSE PHYSICIANS, each for a period of 6 months, falling vacant in January/February, 1958.

Applications, stating age, qualifications, appointment(s) held, and the names of 2 referees, should be sent to the Administrative Officer at the Hospital without delay.

MERTHYR TYDFIL. ST. TYDFIL'S HOSPITAL. Applications are invited for the following posts:

SENIOR HOUSE OFFICER (casualty)
SENIOR HOUSE OFFICER (surgery)

(Latter normally a pre-registration post and due to terminate 31st January, 1958.)

Apply, with full particulars and copies of 2 recent testimonials, to Group Secretary, Merthyr and Aberdare Hospital Management Committee, St. Tydfil's Hospital, Merthyr Tydfil.

MID GLAMORGAN HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the following medical posts which will fall vacant on 1st February, 1958 :—

Neath General Hospital, Neath (412 Beds)
HOUSE SURGEONS.
HOUSE PHYSICIANS.
HOUSE SURGEONS (obstetrics and gynæcology).

Bridgend General Hospital, Quarella-road, Bridgend (381 Beds)
HOUSE SURGEONS.
HOUSE PHYSICIANS.
HOUSE SURGEONS (obstetrics and gynæcology).

These hospitals are recognised by the General Medical Council for pre-registration service.

Applications, naming 2 referees, to be addressed to the Group Secretary of the Committee, 8, Wind-street, Neath.

NORTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. Supernumerary SENIOR REGISTRAR in Thoracic Surgery, Harefield Hospital, Harefield, Middlesex. (616 Beds, including 86 for thoracic surgery, 430 for tuberculosis, and 100 for general medicine and surgery.) Applications are invited from practitioners from overseas (particularly the Commonwealth) with considerable experience in general surgery, who wish to have a period of training in thoracic surgery in England, with the intention of returning subsequently to their own country. Training may include a period spent at Clare Hall Hospital, South Mimms. Appointment in the first instance for 1 year, with eligibility for 1 further year. Resident accommodation available, but appropriate deduction will be made. Hospital may be visited by direct appointment if practicable.

Application forms obtainable from and returnable to Group Secretary, Harefield and Northwood Group Hospital Management Committee, Mount Vernon Hospital, Northwood, Middlesex, by 28th December, 1957.

NEWCASTLE GENERAL HOSPITAL. (836 Beds.) SENIOR HOUSE OFFICER for Pædiatric Department. The post offers experience in the whole of the pædiatric work of the Hospital, including General Medicine and Surgery and Special Departments. There is a close association with the University Department of Child Health.

Applications, together with names and addresses of 2 referees, should be sent to the Secretary, Newcastle General Hospital, Newcastle upon Tyne, 4.

NEWCASTLE REGIONAL HOSPITAL BOARD.

REGISTRAR PSYCHIATRIST, whole-time, resident at St. Luke's Hospital, Middlesbrough (560 Beds). Single or married; furnished or unfurnished accommodation available.

REGISTRAR PSYCHIATRIST, whole-time, St. Mary's Hospital, Stannington, Morpeth (850 Beds). Single accommodation available. Married person may live out by arrangement, if near hospital and prepared to sleep in when on duty.

These appointments offer good experience and training in Psychiatry. Facilities are available for the appointees to take the Durham University D.P.M. Course. Further particulars from Regional Psychiatrist.

Applications, with names and addresses of 3 referees, to Regional Psychiatrist, Newcastle Regional Hospital Board, Benfield-road, Newcastle upon Tyne, 6, within 14 days.

NANTWICH. BARONY HOSPITAL. Registrar (medical) required. Vacant January. Salary and conditions in accordance with Whitley Council scale.

Applications, stating age, qualifications, &c., with names of 2 referees, to be sent to the Group Secretary, South Cheshire Hospital Management Committee, Barony Hospital, Nantwich, Cheshire, within 14 days after publication.

NANTWICH. BARONY HOSPITAL. Senior House OFFICER (medical) required. Vacant February. Salary and conditions in accordance with Whitley Council scale.

Applications, stating age, qualifications, &c., with names of 2 referees, to be sent to the Group Secretary, South Cheshire Hospital Management Committee, Barony Hospital, Nantwich, Cheshire, within 14 days after publication.

NORTHWOOD, MIDDLESEX. MOUNT VERNON HOSPITAL. Applications are invited for Whole-time SURGICAL REGISTRAR from end of February, 1958. Required for 1 year in the first instance. Appointment recognised for the final F.R.C.S. examination. Candidates may visit the Hospital by direct appointment with the Resident Medical Officer.

Application forms obtainable from and returnable to the Group Secretary, Harefield and Northwood Group Hospital Management Committee, Mount Vernon Hospital, Northwood, Middlesex, by 28th December, 1957.

NORTHAMPTON GENERAL HOSPITAL. (500 Beds.) Vacancy 1st February, 1958, for SENIOR HOUSE OFFICER, E.N.T. Department. Recognised for F.R.C.S. and for D.L.O. Appointment to 30th September, 1958, in first instance.

Applications as soon as possible to S. G. HILL, Superintendent.

NOTTINGHAM GENERAL HOSPITAL. 2 Senior House OFFICERS (orthopædic and fracture) required (January and February, 1958). Post offers exceptional experience in traumatic surgery.

Applications, stating age, qualifications and experience, together with copies of testimonials, to be sent to the Group Secretary.

NOTTINGHAM GENERAL HOSPITAL. Senior House OFFICER (surgical) required on 25th January, 1958.

Applications, stating age, qualifications and experience, together with copies of testimonials, to be sent to the Group Secretary, General Hospital, Nottingham.

NOTTINGHAM GENERAL HOSPITAL. Resident pre-registration HOUSE SURGEONS required, 4th February, 5th February.

Applications, stating age, qualifications and experience, together with copies of testimonials, to be sent to the Group Secretary.

OXFORD. UNITED OXFORD HOSPITALS. The Radcliffe INFIRMARY. Applications are invited for the post of REGISTRAR/RESEARCH ASSISTANT to the Accident Service to commence as soon as possible. The duties of this post will be divided equally between the clinical duties of the Registrar appointment, and research work in the Department, under the supervision of the Director of the Accident Service.

Applications, on forms obtainable from the Administrator, Radcliffe Infirmary, Oxford, should be received as soon as possible.

OXFORD. UNITED OXFORD HOSPITALS. Applications are invited for the post of SENIOR HOUSE OFFICER at the Cowley-road Hospital, which is concerned with the treatment of acute and long-stay geriatric patients. This post will be vacant with effect from 1st February, 1958, for 6 months in the first instance.—

Applications, with names of 2 referees, to the Administrator, Radcliffe Infirmary, Oxford, should be received not later than 20th December, 1957.

OXFORD. UNITED OXFORD HOSPITALS. Applications invited for post of NON-RESIDENT REGISTRAR in E.N.T. Department of the Radcliffe Infirmary, for 1 year in the first instance, but eligible for extension to a second year, with effect from 1st February, 1958. Candidates should have passed the Primary examination for the F.R.C.S.

Applications, on forms obtainable from the Administrator, Radcliffe Infirmary, Oxford, should reach him not later than 31st December, 1957.

PLYMOUTH. SOUTH DEVON AND EAST CORNWALL HOSPITAL. Vacancies exist in the following department:—

SENIOR HOUSE OFFICER in Surgery, vacant 17th February, 1958. Recognised for the F.R.C.S.

HOUSE SURGEONS (pre-registration posts), vacancies 9th December, 1957, 1st and 4th January, 1958. Recognised for the F.R.C.S. Greenbank Road Hospital.

In all cases send names of 3 referees to the Group Secretary, 7, Nelson-gardens, Stoke, Plymouth.

PONTEFRACT GENERAL INFIRMARY, Southgate, PONTEFRACT. RESIDENT SURGICAL OFFICER (Senior House Officer grade) required. Hospital approved under F.R.C.S. regulations. Post vacant 1st January, 1958. Married accommodation available.

Applications as soon as possible to the Secretary, Pontefract and Castleford Hospital Management Committee, Great Northern House, Salter-row, Pontefract.

PONTYPRIDD (near). EAST GLAMORGAN HOSPITAL, CHURCH VILLAGE. (316 Beds and large Outpatient Department. Committee's Base Hospital serving population of 174,000. Recognised for D.Obst.R.C.O.G., F.R.C.S., D.C.H., F.F.A.R.C.S., D.A.).

SENIOR HOUSE OFFICER (obstetrics and gynæcology), to commence 13th February, 1958.

SENIOR HOUSE OFFICER (surgery), to commence 1st March, 1958.

2 HOUSE OFFICERS (medicine), to commence 1st February, 1958.

HOUSE OFFICER (pædiatrics), to commence 1st February, 1958.

2 HOUSE OFFICERS (obstetrics), to commence 1st February, 1958.

4 HOUSE OFFICERS (surgery) (to include duties at the Porth and District Hospital), to commence 1st February, 1958.

Applications, stating age, qualifications and experience, together with copies of 2 recent testimonials, to be sent immediately to the Group Secretary, Pontypridd and Rhondda Hospital Management Committee, Courthouse-street, Pontypridd.

PORTSMOUTH GROUP HOSPITAL MANAGEMENT COMMITTEE.

(1) **Saint Mary's Hospital**

(*a*) Applications are invited for the appointment of SENIOR HOUSE OFFICER (medical), vacant now. Duties will be mainly in the acute medical wards and outpatients, but there will be some duties in the Geriatric Assessment Unit of 76 Beds. The appointment affords an opportunity of seeing large numbers of acute cases and is an excellent one for those studying for a higher medical qualification.

(*b*) Surgery (130 surgical beds).

HOUSE OFFICERS (pre-registration) vacant 30th January, 1958, 1st February, 1958, 9th February, 1958, 11th February, 1958.

(*c*) Medical (74 medical beds).

HOUSE OFFICERS (pre-registration), vacant 31st January, 1958, 12th February, 1958.

(2) **Royal Portsmouth Hospital**

(*a*) **Orthopædic Department** (104 beds)

(i) SENIOR HOUSE OFFICER required. Vacant now.

(ii) HOUSE OFFICER (pre-registration). Vacant now.

(*b*) SENIOR HOUSE SURGEON (70 surgical beds). Vacant now.

(*c*) **Medical** (61 medical beds).

HOUSE OFFICERS (pre-registration). Vacant 19th January, 1958, 10th February, 1958.

(3) **Queen Alexandra Hospital**

(*a*) SENIOR HOUSE SURGEON (87 surgical beds). Vacant 1st January, 1958.

(*b*) HOUSE OFFICER. Vacant 12th February, 1958.

(*c*) HOUSE PHYSICIAN (pre-registration) (78 medical beds). Vacant 1st January, 1958.

(*d*) HOUSE OFFICER (pre-registration). Vacant 1st February, 1958.

Applications, stating age, experience and qualifications, together with the names of two referees, should be forwarded as soon as possible to E. H. HURST.

St. Mary's Hospital, Milton-road, Portsmouth.

READING AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE. SENIOR HOUSE OFFICER for E.N.T. Department, Royal Berkshire Hospital, Reading (40 Beds). Post recognised for D.L.O.

Applications, stating age, nationality, experience and qualifications, together with names of 2 referees, should be sent to Group Secretary, 3, Craven-road, Reading.

ROCHESTER, KENT. ST. BARTHOLOMEW'S HOS-PITAL. MEDWAY AND GRAVESEND HOSPITAL MANAGEMENT COMMITTEE. HOUSE SURGEONS. Applications are invited for 2 pre-registration posts, 1 vacant now and 1 vacant mid-January. Salary £467 10s.–£577 10s. p.a. according to experience.

Applications, stating age, qualifications, nationality and experience, to be sent to Hospital Secretary.

ROMFORD, ESSEX. OLDCHURCH HOSPITAL. Resi-DENT PATHOLOGIST (Senior House Officer grade). This post, which will become vacant in the New Year, provides valuable experience by rotation through all departments of this large Group Laboratory and is recognised for the purposes of the Diploma in Pathology. Prospective candidates are invited to visit the Laboratory.

Applications should be sent, with testimonials or the names of 2 referees, as soon as possible to the Secretary, Romford Group Hospital Management Committee, Oldchurch Hospital, Romford.

ROMFORD, ESSEX. RUSH GREEN HOSPITAL. (301 Beds.) RESIDENT HOUSE OFFICER (general surgery) required from 7th January, 1958. Post is recognised for Pre-registration purposes and for F.R.C.S.

Applications should be forwarded immediately to Medical Superintendent stating also names of 2 referees.

RUSTINGTON, SUSSEX. ZACHARY MERTON MATER-NITY HOSPITAL. (54 Beds.) WORTHING GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for a RESIDENT HOUSE OFFICER (preferably Female). Salary £467 10s.–£577 10s. p.a. according to experience, less £125 p.a. for emoluments.

Applications to be submitted to the undersigned immediately.

A. V. OAKTON, Group Secretary,
Worthing Group Hospital Management Committee.
129, Brighton-road, Worthing, Sussex.

SALFORD. HOPE HOSPITAL. Salford Hospital Manage-MENT COMMITTEE. Applications are invited for the post of SECOND RESIDENT CLINICAL PATHOLOGIST, Senior House Officer grade, in the Group Laboratory at Hope Hospital, Salford, which becomes vacant at the end of January, 1958. Post recognised for the Diploma in Pathology.

Applications, together with age, qualifications, and the names and addresses of 2 referees, should be forwarded to the Hospital Secretary.

RYDE. ROYAL I.W. COUNTY HOSPITAL. Isle of WIGHT GROUP HOSPITAL MANAGEMENT COMMITTEE. HOUSE PHYSICIAN required (pre-registration post). Vacant 1st February, 1958.

Applications, with names of 2 referees, to Hospital Secretary not later than 28th December, 1957.

SALISBURY GENERAL HOSPITAL. Applications are invited for the appointment of RESIDENT OBSTETRIC AND GYNÆCOLOGICAL HOUSE SURGEON (recognised by R.C.O.G.)/HOUSE SURGEON for a period of 6 months in each post commencing with House Surgeon post. The posts are open to pre-registration candidates.

Apply immediately, giving names and addresses of 2 referees, to Group Secretary, Salisbury Group Hospital Management Committee, Odstock Hospital, Salisbury.

SALISBURY GENERAL HOSPITAL. Applications are invited for the appointment of RESIDENT HOUSE SURGEON/HOUSE PHYSICIAN to run consecutively in this order from 1st January, 1958, for a period of 6 months in each post. The post is open to pre-registration candidates.

Apply, naming 2 referees, to Group Secretary, Salisbury Group Hospital Management Committee, Odstock Hospital, Salisbury.

SCOTLAND. SOUTH-EASTERN REGIONAL HOS-PITAL BOARD. REGISTRAR to the Royal Edinburgh Hospital for Mental and Nervous Disorders. During the tenure of the post opportunities for study and interchange of training and duty at other centres in the region may be available under the joint training scheme of the South-Eastern Regional Hospital Board and Department of Psychological Medicine of the University of Edinburgh. Single accommodation available. The Hospital may be visited by arrangement with the Physician-Superintendent.

Apply, giving particulars of age, qualifications and previous experience and the names of 2 referees, to the Secretary, 11, Drumsheugh-gardens, Edinburgh, 3, by 28th December.

SCOTLAND. SOUTH-EASTERN REGIONAL HOS-PITAL BOARD. REGISTRAR in Obstetrics and Gynæcology in the Edinburgh Northern Group of hospitals, vacant on 1st February, 1958. The successful candidate will be required to reside at the Eastern General Hospital.

Apply, giving particulars of age, previous experience and qualifications, and the names of 2 referees, to the Secretary, 11, Drumsheugh-gardens, Edinburgh, 3, by 4th January.

SCOTLAND. WESTERN REGIONAL HOSPITAL BOARD. Applications are invited for the following appointments, which will be for 1 year in the first instance:—

SENIOR REGISTRAR in Ear, Nose and Throat Surgery based at the Ear, Nose and Throat Hospital, Glasgow.

REGISTRAR in Medicine based at the Glasgow Royal Infirmary with duties at Belvidere Infectious Diseases Hospital.

REGISTRAR in Ear, Nose and Throat Surgery based at the Glasgow Royal Infirmary with duties possibly at Law Hospital, Carluke.

Applications (12 copies), stating date of birth, qualifications, experience, present appointment, and the names of 3 referees, to reach the Secretary, Western Regional Hospital Board, 64, West Regent-street, Glasgow, C.2, by 28th December, 1957.

SHREWSBURY. CROSS HOUSES HOSPITAL. Obstetric HOUSE SURGEON. Pre-registration post. Vacant mid-January.

Applications, with copy testimonials, to Group Secretary, Shrewsbury Hospital Group, Royal Salop Infirmary, Shrewsbury.

SHREWSBURY. EYE, EAR AND THROAT HOSPITAL. SENIOR HOUSE OFFICER (ophthalmic). Eye Unit, 35 Beds. Post recognised for the D.O.M.S. Vacant 9th February, 1958.

Applications, with copy testimonials, to Group Secretary, Shrewsbury Hospital Group, Royal Salop Infirmary, Shrewsbury.

SHREWSBURY. ROYAL SALOP INFIRMARY/COP-THORNE HOSPITAL. (500 Beds.) HOUSE PHYSICIAN—pre-registration candidates eligible. Vacant 31st January, 1958.

Applications, with copy testimonials, to Group Secretary, Shrewsbury Hospital Group, Royal Salop Infirmary, Shrewsbury.

SHREWSBURY. ROYAL SALOP INFIRMARY. CHILDREN'S UNIT. SENIOR HOUSE OFFICER or HOUSE OFFICER (pædiatric). Recognised for D.C.H. 6-month appointment. The Unit consists of medical, surgical and fever beds. Vacant mid-January, 1958. Married quarters available.

Applications, with copy testimonials, to Group Secretary, Shrewsbury Hospital Group, Royal Salop Infirmary, Shrewsbury.

SHEFFIELD. THE UNITED SHEFFIELD HOSPITALS. Applications invited for the post of ANÆSTHETIC REGISTRAR. The successful candidate will be required to work in any of the units of the United Sheffield Hospitals.

Applications, with the names of 3 referees, should be sent not later than 17th December, 1957, to the Chief Administrative Officer, The United Sheffield Hospitals, West-street, Sheffield, 1.

SHEFFIELD. THE UNITED SHEFFIELD HOSPITALS. CHILDREN'S HOSPITAL/JESSOP HOSPITAL. Applications invited for the resident post of REGISTRAR or SENIOR HOUSE OFFICER at the above Hospitals, in association with the Department of Child Health in the University of Sheffield. The post is a rotating one between the 2 hospitals, alternating with another Registrar, so that the successful candidate will spend half his time in charge of the newborn babies at the Jessop Hospital and half his time in the Professorial Department at the Children's Hospital. Post vacant 1st February, 1958.

Applications, stating age, qualifications and experience, with the names of 3 referees, should be sent not later than 18th December, 1957, to the Chief Administrative Officer, The United Sheffield Hospitals, West-street, Sheffield, 1.

SHEFFIELD. THE UNITED SHEFFIELD HOSPITALS. RESIDENT SENIOR HOUSE OFFICER in Anæsthetics required for the Royal Infirmary.

Applications, stating age, qualifications and experience, with the names of 3 referees (or copy testimonials), should be sent not later than 21st December to the Superintendent, Royal Infirmary, Sheffield, 6.

SHEFFIELD, 5. CITY GENERAL HOSPITAL. DEPARTMENT OF PATHOLOGY, GROUP LABORATORY. Applications are invited for the appointment of SENIOR HOUSE OFFICER (clinical pathology). Resident accommodation is available and optional. Opportunities for training in morbid anatomy, biochemistry, hæmatology and bacteriology. The work of this and the associated hospitals offers excellent experience to graduates who wish to make pathology their permanent career. The post is recognised for the D.Path.

Apply, giving details of age, qualifications, present and previous appointments with dates, and the names of 2 persons to whom reference may be made, to the Group Secretary, Nether Edge Hospital, Sheffield, 11.

SHEFFIELD, 6. KING EDWARD VII ORTHOPÆDIC HOSPITAL. SHEFFIELD NO. 3 HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the appointment of a SENIOR HOUSE OFFICER. The Hospital has 154 Beds, 100 of which are occupied by children. It is a modern unit for the treatment of poliomyelitis and has close contact with a nearby infectious diseases hospital. The post would suit applicants interested in children's diseases, as there is a fair amount of general medical work.

Applications, with names of 2 referees, to Group Secretary, Sheffield No. 3 Hospital Management Committee, Lodge Moor Hospital, Sheffield, 10.

SKIPTON (near). GRASSINGTON HOSPITAL. (208 Beds.) SENIOR HOUSE OFFICER required for the above Hospital, which provides treatment for tuberculous patients, men and women. Accommodation available for single applicants.

Application to Medical Superintendent.

SLOUGH, BUCKINGHAMSHIRE. UPTON HOSPITAL. Locum HOUSE PHYSICIAN required 30th December–12th January.

Applications to Secretary with names of 2 referees.

SLOUGH, BUCKINGHAMSHIRE. UPTON HOSPITAL. HOUSE SURGEON required, 1 of 2. Pre-registration post.

Applications, with names of 2 referees, to Secretary.

SOUTHAMPTON EYE HOSPITAL. (32 Beds. Recognised for D.O. Examination.) RESIDENT SENIOR HOUSE OFFICER required end December.

Applications, with copies of testimonials, should be forwarded as soon as possible to Secretary, Southampton Group Hospital Management Committee, Bullar-street.

SOUTHAMPTON GENERAL HOSPITAL. (474 Beds.) RESIDENT HOUSE SURGEONS (2) required. Pre-registration candidates eligible.

Applications, with copies of recent testimonials, should be forwarded to Group Secretary, Southampton Group Hospital Management Committee, Bullar-street, Southampton.

SOUTHAMPTON GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of SENIOR HOUSE OFFICER (anæsthetics) for the Anæsthetic Department of the Southampton Group of hospitals. Special facilities for working for F.F.A. R.C.S. and D.A.

Applications, with copies of testimonials, should be forwarded as soon as possible to the Group Secretary, Southampton Group Hospital Management Committee, Bullar-street, Southampton.

SOUTHAMPTON. ROYAL SOUTH HANTS HOS-PITAL. (274 Beds.) RESIDENT HOUSE SURGEON required. Pre-registration candidates eligible.

Applications, with copies of recent testimonials, should be forwarded to Group Secretary, Southampton Group Hospital Management Committee, Bullar-street, Southampton.

SOUTHEND-ON-SEA. GENERAL HOSPITAL. Applications are invited for appointment as SENIOR HOUSE OFFICER to the Orthopædic and Fracture Department. Post vacant end of January, 1958. The Orthopædic and Fracture Department is the centre for reference of all cases from a large surrounding area, and the post offers excellent experience in all aspects of orthopædic and traumatic surgery under the supervision of and with instructions from the Consultant-in-charge. Post recognised for the F.R.C.S. Resident or non-resident.

Applications, stating age, qualifications and experience, together with copies of recent testimonials, should be sent to the undersigned by 30th December. J. C. FIELD, Secretary.

SOUTHPORT GENERAL INFIRMARY. (189 Beds. Recognised for pre-registration and F.R.C.S.)

HOUSE PHYSICIAN, General Medicine.
HOUSE PHYSICIAN, General Medicine and Ophthalmology.
HOUSE SURGEON, General Surgery.
HOUSE SURGEON, General Surgery and Gynæcology.

Appointments vacant early January.

Apply, stating age, qualifications, nationality, experience, post required and enclosing 2 copy testimonials, to Group Secretary, Southport and District Hospital Management Committee, Promenade Hospital, Southport.

STAINES HOSPITAL. North West Metropolitan Regional HOSPITAL BOARD. GYNÆCOLOGICAL REGISTRAR (resident) required at above Hospital. Unit has 32 Beds.

Application forms obtainable from and returnable to the Secretary, Staines Group Hospital Management Committee, Ashford Hospital, London-road, Ashford, Middlesex, by 31st December, 1957. Hospital may be visited by direct appointment with the Medical Director of Ashford Hospital.

STOCKTON-ON-TEES. STOCKTON AND THORNABY HOSPITAL. TEES-SIDE HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of SENIOR HOUSE OFFICER in the Casualty Department at the above-named Hospital, which is in the charge of a Senior Casualty Officer. The post, which is vacant shortly, is recognised for the F.R.C.S. examination, and time for study is available.

Applications, stating full details and giving names of 2 referees, should be addressed to the Hospital Secretary.

STRATFORD-ON-AVON HOSPITAL. (163 Beds.) RESIDENT HOUSE SURGEON. New post providing excellent experience.

Applications, with 2 recent testimonials, to Hospital Secretary.

STRATFORD-ON-AVON GENERAL HOSPITAL. (163 Beds.) SENIOR HOUSE OFFICER (Resident Medical Officer) required. Post vacant January, 1958. Duties on medical wards under supervision of Consultant Staff. Appointment gives good experience in general medicine and is suitable for one working for a higher qualification. 2 other resident staff.

Applications, giving qualifications and experience, together with copies of 2 testimonials, to Hospital Secretary.

ST. ALBANS CITY HOSPITAL, St. Albans, Hertford-SHIRE. (384 Beds.) HOUSE SURGEON (House Officer grade) required for 1 of the 2 surgical teams from 19th December, 1957. Post recognised for F.R.C.S. Preference given to candidates seeking post under the Medical Act, 1950.

Applications to Secretary, Mid Herts Group Hospital Management Committee, Bleak House, Catherine-street, St. Albans.

ST. ALBANS, HERTFORDSHIRE. CELL BARNES HOSPITAL. NORTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. REGISTRAR required at above Hospital. This is a modern hospital where 895 mental defectives of all types and ages are under care. Approved for D.P.M. A good pædiatric experience available. Hospital may be visited by direct appointment.

Application forms obtainable from the Group Secretary, Harperbury Hospital, St. Albans, Hertfordshire, and returnable by 21st December, 1957.

STOCKPORT INFIRMARY. Stockport and Buxton Hos-PITAL MANAGEMENT COMMITTEE. Applications are invited for the post of SENIOR HOUSE OFFICER (non-resident Casualty Officer). Hours of duty: 8.30 A.M.–4.30 P.M. Monday–Friday; 8.30 A.M.–12 NOON Saturday. The post is recognised under F.R.C.S. regulations and would suit a candidate wishing to study for higher qualifications. It is vacant 1st January, 1958.

Applications, stating age, qualifications and experience, together with copies of 2 testimonials, to be addressed to the Secretary, Stockport and Buxton Hospital Management Committee, 59B, Shaw-heath, Stockport, Cheshire.

STOCKPORT INFIRMARY, Stockport. (163 Beds.) Applications are invited for the post of SENIOR HOUSE OFFICER (Assistant Resident Surgical Officer) (general and orthopædics), vacant 10th January, 1958. The post is recognised for the F.R.C.S.

Applications, stating age, experience and qualifications, together with copies of 2 testimonials, to be addressed to the Secretary, Stockport and Buxton Hospital Management Committee, 59B, Shaw-heath, Stockport.

STOKE-ON-TRENT. BUCKNALL HOSPITAL. (40 chest beds for children, 84 infectious, 24 pneumoconiosis, 124 chronic sick beds.) Applications are invited for post of RESIDENT JUNIOR HOSPITAL MEDICAL OFFICER, vacant 1st February. Married accommodation available. The person appointed will be associated with all departments of the Hospital and will be required to assist at the pneumoconiosis clinic.

Detailed applications, with copy testimonials, to Physician-Superintendent, at the Hospital.

STOKE-ON-TRENT. CITY GENERAL HOSPITAL. HOUSE OFFICER (pædiatrics) required. Post vacant 14th January. Pre-registration. Hospital recognised for D.C.H.

Detailed applications, with copy testimonials, to Secretary, Hospital Management Committee, Princes-road, Stoke-on-Trent.

STOKE-ON-TRENT. CITY GENERAL HOSPITAL. HOUSE PHYSICIAN required. Pre-registration post vacant mid-January.

Detailed applications, with copy testimonials, to Secretary at the Hospital.

SUNDERLAND. ROYAL INFIRMARY, Durham-road, SUNDERLAND. (300 Beds.) HOUSE OFFICER or SENIOR HOUSE OFFICER (Male) according to experience, required for duties in gynæcology and urological units. Post vacant 24th December. Provisionally registered practitioners may apply.

Apply to Hospital Secretary, giving the names and addresses of 2 referees.

SWANSEA. MOUNT PLEASANT HOSPITAL. (230 Beds.) GLANTAWE HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the resident post of SENIOR HOUSE OFFICER in Obstetrics for the maternity unit of 40 Beds at the above Hospital. The post, which will become vacant on 12th February, 1958, is for a period of 12 months, and is recognised for the D.Obst.R.C.O.G. examination.

Applications, stating age, qualifications and experience, together with copies of 2 recent testimonials, should be sent to the Hospital Secretary not later than 31st December, 1957.

T. E. JONES, Group Secretary.

SWINDON AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE. SWINDON HOSPITALS. Applications invited for post of RESIDENT HOUSE PHYSICIAN in acute medical unit of 64 Beds at St. Margaret's Hospital. Recognised for training under pre-registration internship regulations and vacant on 17th December, 1957.

Full details, with names of 3 referees, to Secretary, 7, Okus-road, Swindon, immediately.

TAPLOW, near MAIDENHEAD. CANADIAN RED CROSS MEMORIAL HOSPITAL. HOUSE SURGEON required for post vacant 21st January. Pre-registration post.

Applications, stating age, qualifications with dates, and copies of 2 testimonials, to Secretary.

TAPLOW, near MAIDENHEAD. CANADIAN RED CROSS MEMORIAL HOSPITAL. HOUSE SURGEON required for post vacant 3rd January. Pre-registration post.

Applications, stating age, qualifications with dates, and copies of 2 testimonials, to Secretary.

TAPLOW, near MAIDENHEAD. CANADIAN RED CROSS MEMORIAL HOSPITAL. Applications invited for post of HOUSE PHYSICIAN to Special Unit for research in juvenile rheumatism. Post offers scope for those interested in research, pædiatrics, rheumatology or cardiology.

Applications, stating age, qualifications and experience, with copies of 2 testimonials, to Secretary.

TAPLOW, near MAIDENHEAD. CANADIAN RED CROSS MEMORIAL HOSPITAL. RESIDENT ANÆSTHETIC REGISTRAR required. Post recognised for F.F.A. R.C.S.

Application forms obtainable from and returnable to Secretary, Windsor Group Hospital Management Committee, Almaroad, Windsor, by 4th January.

TAUNTON AND SOMERSET HOSPITAL. Applications are invited for the post of SENIOR HOUSE OFFICER (casualty and orthopædic), post vacant mid-January, 1958.

Applications, stating age, nationality and qualifications, together with the names of 2 referees, should be forwarded to the Group Secretary, Taunton Hospital Management Committee, Taunton and Somerset Hospital, Musgrove Park Branch, Taunton, Somerset.

TAUNTON (near). Tone Vale Group Hospital Management Committee, NORTON FITZWARREN, near TAUNTON, SOMERSET. Applications are invited for the appointment of JUNIOR HOSPITAL MEDICAL OFFICER with duties mainly at Tone Vale Hospital, a modern psychiatric hospital of 1100 Beds, treating all forms of mental and nervous disorder and including a unit for psychotic children. The post provides an excellent opportunity for postgraduate training in psychiatry, including outpatient clinic work, and particularly the study of child psychiatry not only with psychotic children in the unit at the Hospital but also attendance at child guidance clinics in the county. Every facility is provided for study for the D.P.M. and facilities are also available for research and opportunities for work for the M.D. degree. Previous holders of this post have been granted special study leave. Accommodation at a moderate charge is available for single or married officer. The appointment will, in the first instance, be limited to 3 years and will be subject to the terms and conditions of service for hospital medical staffs (present salary scale £852 10s.–£1182 10s. p.a.).

Applications, giving details of age, qualifications and experience, together with the names and addresses of 2 referees, should be forwarded to the Group Secretary within 10 days of the appearance of this advertisement.

TEES-SIDE HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of SENIOR HOUSE OFFICER (anæsthetics) with the above-named Group of hospitals. Main duties at North Ormesby and Eston Hospitals. Post recognised for D.A. and F.F.A. R.C.S. Some experience in anæsthetics an advantage though not essential.

Applications, with copies of 3 testimonials, to the Group Secretary, Tees-side Hospital Management Committee, North Ormesby Hospital, Middlesbrough, within 14 days.

TORQUAY. TORBAY HOSPITAL. (166 general beds.) RESIDENT HOUSE OFFICER (surgical), Male or Female, required approximately 15th December, 1957. Post recognised for F.R.C.S. and pre-registration purposes. There is a complement of 6 Resident House Officers.

Applications, stating qualifications, nationality and age, together with copy testimonials (quoting reference F.955/84), to the Group Secretary, Torquay District Hospital Management Committee, Torbay Hospital, Torquay, S. Devon.

TORQUAY. TORBAY HOSPITAL. Resident Casualty OFFICER (Senior House Officer status) required approximately 23rd December, 1957. There is a complement of 6 Resident House Officers.

Applications, stating qualifications, nationality, age (quoting ref. F.955/86), with copy testimonials, to the Group Secretary, Torquay District Hospital Management Committee, Torbay Hospital, Torquay, S. Devon.

TREDEGAR GENERAL HOSPITAL, MONMOUTHSHIRE. RHYMNEY AND SIRHOWY VALLEYS HOSPITAL MANAGEMENT COMMITTEE. RESIDENT SURGICAL OFFICER (Senior House Officer or Junior Hospital Medical Officer grade according to experience) required for Surgical Unit at above Hospital. Duties are those of Assistant to General Surgeon; staff, includes House Surgeon. Commodious family flat.

Apply, with full particulars and stating names of 2 referees, to Secretary.

TUNBRIDGE WELLS. KENT AND SUSSEX HOSPITAL. (303 Beds.) TUNBRIDGE WELLS GROUP HOSPITAL MANAGEMENT COMMITTEE. SENIOR HOUSE OFFICER (anæsthetics) required (Male or Female), resident. Vacant 13th January, 1958. Recognised D.A. and F.F.A. R.C.S.

Applications, giving age, qualifications and experience, with names of 2 referees, to Group Secretary, Sherwood Park, Pembury-road, Tunbridge Wells.

TUNBRIDGE WELLS (near). PEMBURY HOSPITAL, PEMBURY. Applications invited for appointment of SENIOR ORTHOPÆDIC HOUSE SURGEON AND CASUALTY OFFICER (Senior House Officer grade) to begin duties as soon as possible. Recognised F.R.C.S. (Eng.) and tenable for 1 year. Work includes treatment of long and short stay cases and traumatic surgery with large Outpatient and Fracture Clinics under 2 Consultants.

Apply, stating age, qualifications and experience, together with 3 testimonials, to Group Secretary, Sherwood Park, Pembury-road, Tunbridge Wells.

TYNEMOUTH VICTORIA JUBILEE INFIRMARY. (115 Beds.) RESIDENT HOUSE SURGEON (orthopædic), Junior Hospital Medical Officer or Senior House Officer grade according to experience. Post is also recognised for pre-registration purposes.

Applications, with names of 2 referees, to Group Secretary, Preston Hospital, North Shields.

WOODFORD GREEN, ESSEX. HARTS HOSPITAL. (100 Beds.) SENIOR HOUSE OFFICER required, post vacant 12th January, 1958. The Hospital is a modern sanatorium with Area Chest Clinic. The post offers exceptional opportunities for gaining experience in tuberculosis and diseases of the chest. Accommodation for single person only. Salary £819 10s. p.a., less £150 p.a. for board, lodging, &c.

Applications, with copies of 2 recent testimonials, should be sent immediately to Secretary, Forest Group Hospital Management Committee, Langthorne-road, E.11.

WATFORD, HERTFORDSHIRE. PEACE MEMORIAL HOSPITAL. (211 Beds.) Applications are invited for the post of HOUSE SURGEON at the above Hospital. This is a pre-registration post and is recognised for F.R.C.S. Salary according to the National Health Service scale.

Applications, with copies of recent testimonials to the Administrator.

WATFORD, HERTFORDSHIRE. PEACE MEMORIAL HOSPITAL. (211 Beds.) ORTHOPÆDIC HOUSE SURGEON (with certain casualty duties) required. Post recognised for F.R.C.S.(Eng.) examination. Intermediate or senior post, depending on experience for orthopædic unit (30 Beds). The orthopædic service is in charge of a Consultant and Registrar closely associated with a postgraduate teaching hospital.

Applications with copies of 2 testimonials to the Administrator.

WALSALL HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the following appointments :—

Manor Hospital (340 Beds)
HOUSE SURGEON
HOUSE PHYSICIAN.
PÆDIATRIC HOUSE PHYSICIAN required, 1st February, 1958. Recognised for D.C.H.

General Hospital (181 Beds)
HOUSE SURGEON.
HOUSE PHYSICIAN.

All posts recognised for pre-registration.

Applications, together with names of 2 referees, to Group Secretary, Walsall General (Sister Dora) Hospital.

WARWICK HOSPITAL. (320 Beds.) House Surgeon. Pre-registration or registered candidates may apply. Good experience in general surgery. Vacant 25th January, 1958. Married quarters available.

Applications, with 2 testimonials, to be forwarded to the Medical Superintendent.

WARWICK (near). CENTRAL MENTAL HOSPITAL (1400 Beds.) SENIOR HOUSE OFFICER. Neurosis unit, adult and child psychiatry clinics, departments of electroencephalography, occupational therapy, psychology and social work. Recognised for D.P.M. Accommodation available. Post available mid January.

Applications, with names and addresses of 3 referees, to Medical Superintendent by 24th December.

WEST CUMBERLAND HOSPITAL MANAGEMENT COMMITTEE. JUNIOR HOSPITAL MEDICAL OFFICER in Anæsthetics required for work throughout the West Cumberland Group but based on Whitehaven Hospital. Good experience essential, and possession of the D.A. preferred.

Apply, with full information as to qualifications and experience, and giving the names of 2 referees, to the Group Secretary at Workington Infirmary.

WELSH REGIONAL HOSPITAL BOARD. Registrar (thoracic medicine), Llangwyfan Hospital, near Denbigh. Modern methods of treatment tuberculosis. 370 adult beds (male and female) and children. Hospital also contains major thoracic unit. Subject to review end of first year.

Forms of application from Senior Administrative Medical Officer, Temple of Peace, Cathays Park, Cardiff, within 14 days.

WESTON-SUPER-MARE GENERAL HOSPITAL. (107 Beds.) Applications are invited from registered medical practitioners for the pre-registration appointment (resident) of HOUSE PHYSICIAN, vacant 1st February, 1958.

Applications, stating age, qualifications, together with names and addresses of 2 referees, should be addressed to the Secretary, Weston-super-Mare Hospital Management Committee.

WESTON-SUPER-MARE GENERAL HOSPITAL. (107 Beds.) Applications are invited from registered medical practitioners for the pre-registration appointment (resident) of HOUSE SURGEON, vacant 1st February, 1958.

Applications, stating age, qualifications, together with names and addresses of 2 referees, should be addressed to the Secretary, Weston-super-Mare Hospital Management Committee.

WINDSOR. KING EDWARD VII HOSPITAL. House SURGEON in General Surgery required, Male or Female, for post vacant 18th January. Pre-registration post, recognised for F.R.C.S.

Applications, stating age, nationality, qualifications with dates, and copies of recent testimonials, to Secretary.

WOLVERHAMPTON. NEW CROSS HOSPITAL. (634 Beds.) Pre-registration HOUSE OFFICERS in General Surgery. Vacant January.

Applications to Hospital Secretary.

WOLVERHAMPTON. NEW CROSS HOSPITAL. (634 Beds.) SENIOR HOUSE OFFICERS or HOUSE OFFICERS (pre-registration) in Medicine. Acute medical beds. Vacant January.

Applications to Hospital Secretary.

WOLVERHAMPTON. THE ROYAL HOSPITAL. (An Associated Hospital of the Birmingham University Medical School.) HOUSE OFFICER (pre-registration) E.N.T. Department, recognised for the D.L.O. and F.R.C.S. examinations. Vacant 1st March.

Apply, giving age and qualifications, with copies of 2 testimonials, to the Hospital Secretary.

NORTHERN IRELAND HOSPITALS AUTHORITY. Applications are invited for a whole-time post as SENIOR TUTOR/SENIOR REGISTRAR in General Surgery at hospitals managed by the Belfast Hospital Management Committee. In the first instance the appointment will be for the period ending 30th September, 1958, and will be made jointly by the Authority and the Queen's University, Belfast. The appointment will involve teaching and other University duties as Senior Tutor in the Department of Surgery.

Applications should be made on a form which may be obtained (with further particulars) from the Secretary, Northern Ireland Hospitals Authority, 44/46, Queen-street, Belfast, and which must be returned so as to be received notlater than 23rd December, 1957.

WORCESTER ROYAL INFIRMARY. (213 Beds.) Applications are invited for the post of SENIOR HOUSE OFFICER in Medicine (Resident Medical Officer), vacant early January. The post is of 1 year's duration and besides acute medicine the post covers some work in infectious diseases and geriatrics.

Applications, with copies of 3 recent testimonials, to be sent to the Secretary.

B.W.I. UNIVERSITY COLLEGE HOSPITAL OF THE WEST INDIES. Applications are invited for the post of SENIOR REGISTRAR or REGISTRAR in the Division of Obstetrics and Gynæcology at the above named Teaching Hospital. This post which is resident is recognised for training for membership of the Royal College of Obstetricians and Gynæcologists. The post will be vacant on 1st January, 1958. The appointment will be for 1 year in the first instance. Salary is in the scale £900–£100–£1100 : £1200–£100–£1500 p.a. depending on qualifications and experience. Single accommodation and board may be provided at a deduction from salary at the rate of £145 p.a. or, if available, an unfurnished flat may be provided at a rental of 5% of salary. Passages by sea will be paid from the country of recruitment for 1 person only for this appointment.

Further information may be obtained from the Hospital Manager and Secretary, University College Hospital of the West Indies, Mona, Jamaica, B.W.I., to whom applications stating age, nationality, details of experience and qualifications, together with 3 recent testimonials or the names and addresses of 3 referees, should be sent not later than 31st December, 1957.

MICHIGAN, U.S.A. OAKWOOD HOSPITAL, Dearborn, MICHIGAN. Applications are invited for 1 or 2-year approved GENERAL PRACTICE RESIDENCY in modern 234-Bed General Hospital 10 miles from Detroit. Excellent facilities. Hospital approved for exchange-visitor programme. Beginning monthly salary $250 if single, $300 if married. Free housing. Apply: Director.

Public Appointments

BRITISH RAILWAYS (Scottish Region). Applications are invited from registered medical practitioners (Male), preferably aged 28 to 35, for the appointment of Full-time ASSISTANT MEDICAL OFFICER. The successful candidate will work initially in Glasgow and will be required to travel to visiting centres for a few days each month ; and must be prepared to transfer elsewhere in the Region if required. Candidates should have a good clinical background and an interest in industrial medicine. Commencing salary in the region of £1400 p.a. Superannuation fund membership, subject to medical examination is obligatory.

Applications, with particulars of age, qualifications and experience, together with the names of 2 referees, should be sent to the Regional Medical Officer, British Railways (Scottish Region), 54, George-square, Glasgow, C.2, not later than 31st December, 1957.

GREAT YARMOUTH. COUNTY BOROUGH OF GREAT YARMOUTH. DEPUTY MEDICAL OFFICER OF HEALTH/SCHOOL MEDICAL OFFICER/DEPUTY PORT MEDICAL OFFICER. Applications are invited from registered medical practitioners, holding a qualification in public health, for the above superannuable appointment. Candidates should have had experience in general public and school health work and be capable of assuming full responsibility for the Health Department in the absence of the Medical Officer of Health. Experience in infectious diseases and the ascertainment of educationally subnormal pupils will be considered additional qualifications. The salary will be within the scale £1266 p.a. rising by annual increments of £55 to a maximum of £1596, plus a car allowance which at present is at the rate of £180 p.a. The appointment may be terminated by 3 months' notice on either side. Housing accommodation will be made available by the Council, if required.

Further details regarding the appointment and the submission of applications may be obtained from the undersigned, by whom applications should be received not later than 28th December, 1957. FARRA CONWAY, Town Clerk.

Town Hall, Great Yarmouth.

NORTHUMBERLAND. COUNTY OF NORTHUMBERLAND. Joint appointment of AREA EXECUTIVE MEDICAL OFFICER for the South East Area and MEDICAL OFFICER OF HEALTH for the Borough of Whitley Bay and the Urban Districts of Longbenton and Seaton Valley. Applications are invited from registered medical practitioners for the joint appointment of Area Executive Medical Officer for the South East Area and Medical Officer of Health for the Borough of Whitley Bay and the Urban Districts of Longbenton and Seaton Valley. The salary for the joint appointment will commence at £1928 15s., rising by 4 annual increments of £65 and 1 of £25 to £2213 15s., plus a travelling allowance in respect of a motorcar not exceeding 12 h.p. The person appointed will be required to give his, or her, whole time to the duties of the joint appointment and must not engage directly or indirectly in private practice. The appointment is subject to the provisions of the Local Government Superannuation Acts, to the national conditions of service, and to 3 months' notice in writing on either side, and the successful candidate will be required to pass a medical examination.

Application forms and further particulars may be obtained from the Clerk of the County Council, County Hall, Newcastle upon Tyne, 1, to whom applications must be submitted not later than 23rd December, 1957.

SURREY COUNTY COUNCIL. Appointment of Assistant MEDICAL OFFICER. Applications are invited from candidates possessing the D.P.H. or D.C.H. Main duties will be in connection with the school health and maternity and child welfare service. Salary according to experience, on the scale £1050–£50–£1200–£55–£1475 p.a. The appointment is subject to the provisions of the Local Government Superannuation Acts, 1937/1953 and to 3 months' notice on either side.

Application form from the County Medical Officer, County Hall, Kingston-upon-Thames, to be returned by 28th December, 1957.

GATESHEAD. COUNTY BOROUGH OF GATESHEAD. Applications for the appointment of DEPUTY MEDICAL OFFICER OF HEALTH AND DEPUTY PRINCIPAL SCHOOL MEDICAL OFFICER are invited from registered medical practitioners, who hold a Diploma in Public Health. Candidates should have had experience in all branches of the Public Health and School Health Services. Salary £1380–£55 (4)–£1600–£50 (1)–£1650 p.a. The appointment is superannuable, subject to medical examination, and is terminable by 3 months' notice on either side.

A list of the duties of the office may be obtained from the Medical Officer of Health, Greenesfield House, Mulgrave-terrace, Gateshead, to whom applications, stating age and experience and accompanied by the names of not more than 3 persons to whom reference can be made, should be sent in envelopes endorsed "Deputy Medical Officer" within 14 days of the appearance of this advertisement. C. D. JACKSON, Town Clerk.

Town Hall, Gateshead, 8, 2nd December, 1957.

GLOUCESTERSHIRE COUNTY COUNCIL. Kingswood AND MANGOTSFIELD URBAN COUNCILS AND SODBURY AND WARMLEY RURAL COUNCILS. Applications are invited for the appointment of DIVISIONAL MEDICAL OFFICER OF HEALTH AND MEDICAL OFFICER OF HEALTH, which is whole-time and involves an approximately equal distribution of duties between the County Council and the 4 County District Councils. The salary is in accordance with the Medical Council of the Whitley Council for the Health Services and is £918 15s. rising by 1 annual increment of £31 5s. and 7 of £34 7s. 6d. to £1190 12s. 6d. in respect of County Council duties, and £975 rising by 4 annual increments of £27 10s. and 1 of £25 to £1110 in respect of District Council duties. The selected candidate will be required to provide a motorcar; travelling expenses payable on approved scale. The appointment is superannuable and the passing of a medical examination will be necessary. Applicants must hold a Diploma in Public Health and in respect of the County Council duties will act under the direction of the County Medical Officer of Health. The appointment will be subject to 3 calendar months' notice, in writing, on either side.

Applications, stating age, qualifications and previous experience, together with the names of 2 persons to whom reference may be made, should be sent to Clerk of the South Gloucestershire (M.O.H.) Joint Committee, The Council Offices, Hollow-road, Kingswood, Bristol, not later than 4th January, 1958.

GUY H. DAVIS,
Clerk of the County Council.
J. H. DEARNLEY,
Clerk of the South Gloucestershire
(M.O.H.) Joint Committee.

YORKSHIRE. COUNTY COUNCIL OF THE WEST RIDING OF YORKSHIRE. Applications are invited from registered medical practitioners, Men or Women, for the post of ASSISTANT COUNTY MEDICAL OFFICER AND SCHOOL MEDICAL OFFICER in the Castleford area of the County. The Assistant will be on the staff of the County Medical Officer's Department but will work under the administrative direction of the Divisional Medical Officer for the area. The duties will be mainly clinical in the School Health and Infant Welfare Services, but other County health duties may be included by the Divisional Medical Officer. The scale of salary is £1050–£1475 p.a. A minimum of 3 years' experience since qulification is desirable and the possession of a Diploma in Child Health will be an advantage. Travelling and subsistence allowances according to the County Council's scale are payable in addition to salary. The post is superannuable and the successful applicant will be required to pass a medical examination as to physical fitness.

Forms of application can be obtained from the undersigned, to whom they should be returned not later than 30th December, 1957. J. WOOD-WILSON, County Medical Officer.

County Hall, Wakefield.

GOVERNMENT OF THE FEDERATION OF NIGERIA. MEDICAL OFFICER OF HEALTH required for administration of Public Health and control of sanitary matters, or if posted to sea or airport, the duties of Port Health Officer. May be required to perform general duties of Medical and Health Officer and other duties in connection with epidemic diseases. Must possess medical qualifications registrable in the United Kingdom and D.P.H. Appointment :—

(*a*) On short-term contract with inclusive salary from £1536 to £2286 p.a. On completion of contract gratuity (taxable) is paid of £37 10s. for each completed period of 3 months' service (including leave).

(*b*) From National Health Service with inclusive salary from £1326 to £1950 p.a., candidate retaining superannuation rights and receiving gratuity (taxable) of 20% of aggregate of salary.

Quarters at low rental. Free return passages for officer and wife. Return passages for children, to age 18, provided cost does not exceed that of 2 adult return passages in any 1 tour of service. Children's (separate domicile) allowance of £75 a year for each child under 18, ceasing if children join parents in Nigeria. Income-tax at local rates. Local leave permissible and generous home leave after each tour.

Application forms from Director of Recruitment, Colonial Office, London, S.W.1 (quoting BCD. 117/14/07).

HER MAJESTY'S OVERSEAS CIVIL SERVICE. Somaliland Protectorate. MEDICAL OFFICER with qualifications registrable in United Kingdom required for general medical duties, including simple surgery and, if necessary, training of dressers. Salary scale from £1116–£1836 a year, plus temporary (non-pensionable) cost of living allowance of 10% of salary subject to maximum of £162. Commencing salary determined by qualifications and experience. Pension earned at rate of 1/600th of final pensionable emoluments for each completed month of service. Furnished quarters at low rental. Free passages in both directions for officer, wife and up to 4 children under 18 years. No income tax. Tour of service 15–21 months, after which generous home leave granted. Local leave also granted.

Application forms from Director of Recruitment, Colonial Office, London, S.W.1 (quoting BCD. 117/5/01).

HER MAJESTY'S OVERSEAS CIVIL SERVICE. DOMINICA, WINDWARD ISLANDS. DISTRICT MEDICAL OFFICERS required for general duties in Dominica, with liability for service in any Institution, Dispensary, or District within the Windward Islands. Candidates must hold qualification registrable in United Kingdom. Appointment on permanent basis with pension (non-contributory) or on agreement for 3 years. Salary scale, including pay additions, £960–£1200 a year. Pension 1/600th of final pensionable emoluments for each completed month of service. Income-tax at local rates. Private practice as far as duties permit. Travel and subsistence allowances in accordance with local regulations. Quarters not normally provided but if Government quarters become available rental of 10 % of salary, or 5 % of assessed value of quarters, whichever is less, will be charged. Free passages on appointment for officer, wife and dependent children under 18 years not exceeding 5 persons in all. If appointed on contract, free return passages on completion of contract. Leave passages in accordance with Windward Islands Regulations. Only permanent officers become members of Her Majesty's Overseas Civil Service.

Application forms from Director of Recruitment, Colonial Office, London, S.W.1 (quoting BCD. 117/40/01).

PERTH PRISON. Medical Officer (Part-time). Work includes visits of approximately 1 hour daily except Sundays: emergency calls: occasional hygiene inspections and reports. Medical Officer must supply a deputy when he is not available. Salary £600 p.a. (not superannuable).

Application forms from the Director of Prison and Borstal Services, Government Buildings, Broomhouse-drive, Saughton, Edinburgh, 11.

DUBLIN. LOCAL APPOINTMENTS COMMISSION. Vacancies for ANÆSTHETISTS.

1. Anæsthetist (whole-time), Western Health Institutions Board. Inclusive salary £2114. Essential qualifications include (*a*) a recognised Diploma in Anæsthetics or equivalent and (*b*) 5 years' specialisation in the practice of anæsthetics and experience in the administration of anæsthetics for thoracic surgical cases.

2. Anæsthetist (whole-time), Board of Public Assistance for the South Cork Public Assistance District. Inclusive salary £2114. The person appointed may undertake, if offered, a University teaching appointment. Essential qualifications include (*a*) a recognised Diploma in Anæsthetics or equivalent and (*b*) 5 years' specialisation in the practice of anæsthetics.

3. Anæsthetists (part-time), (*a*) Tipperary (S.R.), (*b*) Cavan County Councils. Basic salary for each post: £809. Additional payment for attendance exceeding 15 hours a week. Essential qualifications include (*a*) a recognised Diploma in Anæsthetics or equivalent and (*b*) adequate experience in the administration of anæsthetics.

Application forms and further particulars from the Secretary, 45, Upper O'Connell-street, Dublin. Latest time for receiving completed application forms: 5 P.M. on 7th January, 1958.

BASUTOLAND AND SWAZILAND PROTECTORATES. MEDICAL OFFICERS with qualifications registrable in United Kingdom required for general duties. "R" practitioners, i.e., practitioners liable for call-up under the National Service Acts may apply, and if appointed, will be granted indefinite deferment of call-up on completion of a minimum period of 2 years. Appointment on 2 years' probation to the pensionable establishment. Salary £940–£1515 a year, starting-point determined by age and experience. Following also payable: —

(*a*) Cost of living allowance of 15½ % of salary up to maximum of £170 10s. a year for married officers and half this rate for single officers.

(*b*) Education allowance (up to 3 children under the age of 18 attending school outside territory) of £120 a year for first child, £96 for second, and £72 for third.

Free passages for officer, wife and up to 3 children. Local leave permitted and generous home leave granted after each tour of 36 months. Income-tax at low local rates.

Application forms from Director of Recruitment, Colonial Office, London, S.W.1 (quoting BCD. 117/76/01).

General Practice

For an ***Executive Council post*** *(England and Wales) apply on form* E.C.16A *obtainable from the council. Mark envelope "Vacancy."*

HOYLAKE, CHESHIRE. Applications are invited for VACANCY due to retirement. Duties to commence 1st April, 1958. Urban area. List at present approximately 1120. House and surgery probably available. Applications on Form E.C.16A to be submitted not later than 28th December, 1957, to the Clerk of the Cheshire Executive Council, 28, Nicholas-street, Chester.

HAZEL GROVE, CHESHIRE. Applications are invited for VACANCY due to death of practitioner. Mainly Urban area. List at present approximately 2580. House and surgery probably available. Applications on Form E.C.16A to be submitted not later than 28th December, 1957, to the Clerk of the Cheshire Executive Council, 28, Nicholas-street, Chester.

Hospital Services: Non-Medical Appointments

MANCHESTER. UNITED MANCHESTER HOSPITALS. MANCHESTER ROYAL INFIRMARY. A vacancy exists for a MEDICAL PHOTOGRAPHER in the Department of Medical Illustration. Whitley Council conditions of salary and service, £440–£20 (4)–£25 (1)–£545 p.a.

Applications, together with the names of 2 referees, to the Secretary, Manchester Royal Infirmary, Manchester, 13.

Miscellaneous

Histologic technicians, experienced. Excellent salary. —Write Congenital Heart Disease Research and Training Center, 629, South Wood-street, Chicago, Ill., U.S.A., giving full details.

THE UNIVERSITY OF MANCHESTER. Applications are invited for the post of Assistant Medical Artist, who should be suitably qualified and who will work under the direction of the Medical Artist in the preparation of paintings, drawings, diagrams and similar works for members of the staff of the Medical School, both in the University and in the United Manchester Hospitals. Applicants should have had art training, together with at least 2 years' study and training at a University or Teaching Hospital, under a Medical Artist. Starting salary £450 p.a. rising by annual increments of £25 to £500 p.a. Duties to begin in January, 1958, or as early as possible thereafter.

Applications should be sent not later than 31st December, 1957, to the Registrar, the University, Manchester, 13, from whom further particulars may be obtained. Applicants should give the names of not more than 3 persons to whom reference may be made and may also submit copies of not more than 3 testimonials which will *not* be returned.

Principal M.O. required for a large group of tea gardens in north east India early May, 1958, for 6 months. Operating surgical experience required. Would suit man reading for final F.R.C.S. Furnished bungalow, servants and transport provided. Free return passages for doctor and wife.—Apply with full details, qualifications and experience and recent testimonials to Address No. 355, THE LANCET Office, 7, Adam-street, Adelphi, London, W.C.2.

Required, Assistant Medical Officer (preferably about 30 years of age) for large chemical factory in Yorkshire. Exceptional opportunities for young man keen on toxicology and general industrial medical practice. Salary according to qualifications and experience, minimum £1400 p.a. Applications in writing to Staff Department, Imperial Chemical Industries Limited, Dyestuffs Division, Hexagon House, Blackley, Manchester, 9.

Korea. Doctor (Female) required with paediatric experience; age preferably between 26 and 40. Contract 1 year renewable. Salary £1000 p.a. Maintenance equipment allowances and fares paid. 1 month's holiday per year. Duties in Pusan, Korea.—Apply Foreign Relief Secretary, Save the Children Fund, 12, Upper Belgrave-street, S.W.1. Telephone SLOane 9171.

Esso Petroleum Company, Limited, have a vacancy in their Medical Department for an Industrial Hygiene Engineer. His function will be to investigate and advise on all health hazards arising from the company's operations, including the handling and use of products. Candidates should hold a degree or its equivalent in chemical engineering, chemistry or a similar field. Experience or training in industrial hygiene or sanitary engineering would be an advantage. Candidates between ages 25–35 may write for further particulars to Personnel Manager, Esso Petroleum Company, Limited, 16, Charles II-street, Haymarket, S.W.1.

PARKE, DAVIS AND COMPANY LIMITED

seek to extend their

CLINICAL INVESTIGATION DEPARTMENT

Applications are therefore invited from medically qualified personnel for this purpose. The duties involved include the direction of clinical investigation on potential new drugs in Britain and Europe. Applicants must be well qualified, age about 30–40, active, and with a broad range of medical interests. Experience in clinical research would be an advantage as would some knowledge of European languages. Salary paid would depend on qualifications, experience, &c., but would not be less than £1750 p.a. A comprehensive pension plan is in operation. Application with full details of career, &c., should be made to The Deputy General Manager, Parke, Davis and Company, Limited, Staines-road, Hounslow.

Australian cash buyer wants House Practice, Southern England Country area. Suitable, husband, wife. General practice and obstetrics.—Address, no. 356, THE LANCET Office, 7, Adam-street, Adelphi, London, W.C.2, first instance, strict confidence. Long locum considered.

For Sale. Established medical practice in desirable South Island area, New Zealand. Gross turnover approximately £6000. Practice includes plant and equipment and interest in clinic. Also house and contents. Approximately £8000 capital required. Vendor would assist with finance.—Replies to: "Medical Practice," c/o Charles Haines Advertising Ltd., P.O. Box 1490, Wellington, New Zealand.

"Alfona" is fat-free cow's milk to which has been added vegetable oils containing essential fatty acids suitable for atheroma cases.—Enquiries to ALFONAL, Shell-Mex House, Strand, London, W.C.2. (Telephone COV. 2211.)

Doctors requiring applications, theses copied: Write to MANTON (WESTMINSTER) LTD., 98, Victoria-street, S.W.1 (VIC 0141), who are specialists.

Medical Books: Our Catalogue 705: Medical books and periodicals, second-hand, new and forthcoming: 100 pp.: free on application.—HEFFER'S, Petty Cury, Cambridge.

"Pregnancy Diagnosis by the Xenopus Method," 24-hour service. Send specimens of urine and £2 2s. fee. Hæmatology, Biochemistry, Flame Photometry.—WELBECK BIOLOGICAL LABORATORIES, 26, Park-crescent, Portland-place, W.1 (MUSeum 5386–7).

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The original Lente Insulins

NOVO

Novo Lente Insulin

Novo Semilente Insulin

Novo Ultralente Insulin

All available in 40 and 80 units per ml.

EVANS MEDICAL

EVANS MEDICAL SUPPLIES LTD.

SPEKE, LIVERPOOL 19 (HUNTS CROSS 1881)

London Office: Ruislip, Middlesex (Ruislip 3333)

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Aspirin Sensitivity?

Constipation, gastric irritation, allergy and other undesirable side effects may follow the use of analgesics based on the aspirin-codeine-phenacetin formula. Panadol does not contain any of these substances but has the single active ingredient N-acetyl-p-aminophenol. It does not cause gastric irritation or constipation and may safely be given to patients with peptic ulcer and to those who are intolerant of other analgesics.

Medical literature is available on request.

Panadol

is safe for everyone

Tablets: 0.5 G., N-acetyl-p-aminophenol. In cartons of 20, in bottles of 100 and 500, and in tins of 2500.
Basic N.H.S. cost of continuous treatment (2 tabs. t.d.s.) for one week 3/5.

Bayer Products Limited
Neville House, Kingston-on-Thames, Surrey.
Associated exporting company: Winthrop Products Limited

BAYER

PANADOL is a registered trade mark.